“BASAL CELL CARCINOMA – A PROSPECTIVE CLINICO EPIDEMIOLOGICAL & PATHOLOGICAL STUDY”

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(BRANCH XX)

MADRAS MEDICAL COLLEGE

THE TAMILNADU DR. M.G.R. MEDICALUNIVERSITY

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CERTIFICATE

Certified that this dissertation titled **"BASAL CELL CARCINOMA - A PROSPECTIVE CLINICO EPIDEMIOLOGICAL & PATHOLOGICAL STUDY"** is a bonafide work done by **Dr.V.AMMASAIGOUNDAN,** Post-graduate student of the Department of Dermatology, Venereology and Leprosy, Madras Medical College, Chennai – 3, during the academic year 2013 – 2016. This work has not previously formed the basis for the award of any degree.

Prof. A. RAMESH, M.D.,D.D.,
Professor
Department of Dermatology
Madras medical college/RGGGH
Chennai-3

Prof. K. MANOHARAN, M.D.,D.D.,
Prof and Head of the Department
Department of Dermatology
Madras Medical College/RGGGH
Chennai-3.

Prof. Dr.R.VIMALA, M.D.,
Dean
Madras Medical College
Chennai – 3

DECLARATION

I, **Dr. V. AMMASAIGOUNDAN** solemnly declare that this dissertation titled **"BASAL CELL CARCINOMA – A PROSPECTIVE CLINICO EPIDEMIOLOGICAL & PATHOLOGICAL STUDY"** is a bonafide work done by me at Madras Medical College during 2013-2016 under the guidance and supervision of **Prof.K.MANOHARAN, M.D.,D.D.,** Professor and head of the department of Dermatology, Madras Medical College, Chennai-600003.

This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai towards partial fulfillment of the rules and regulations for the award of **M.D Degree in Dermatology, Venereology and Leprosy (BRANCH-XX)**

Place :

Date : **(DR.V.AMMASAIGOUNDAN)**

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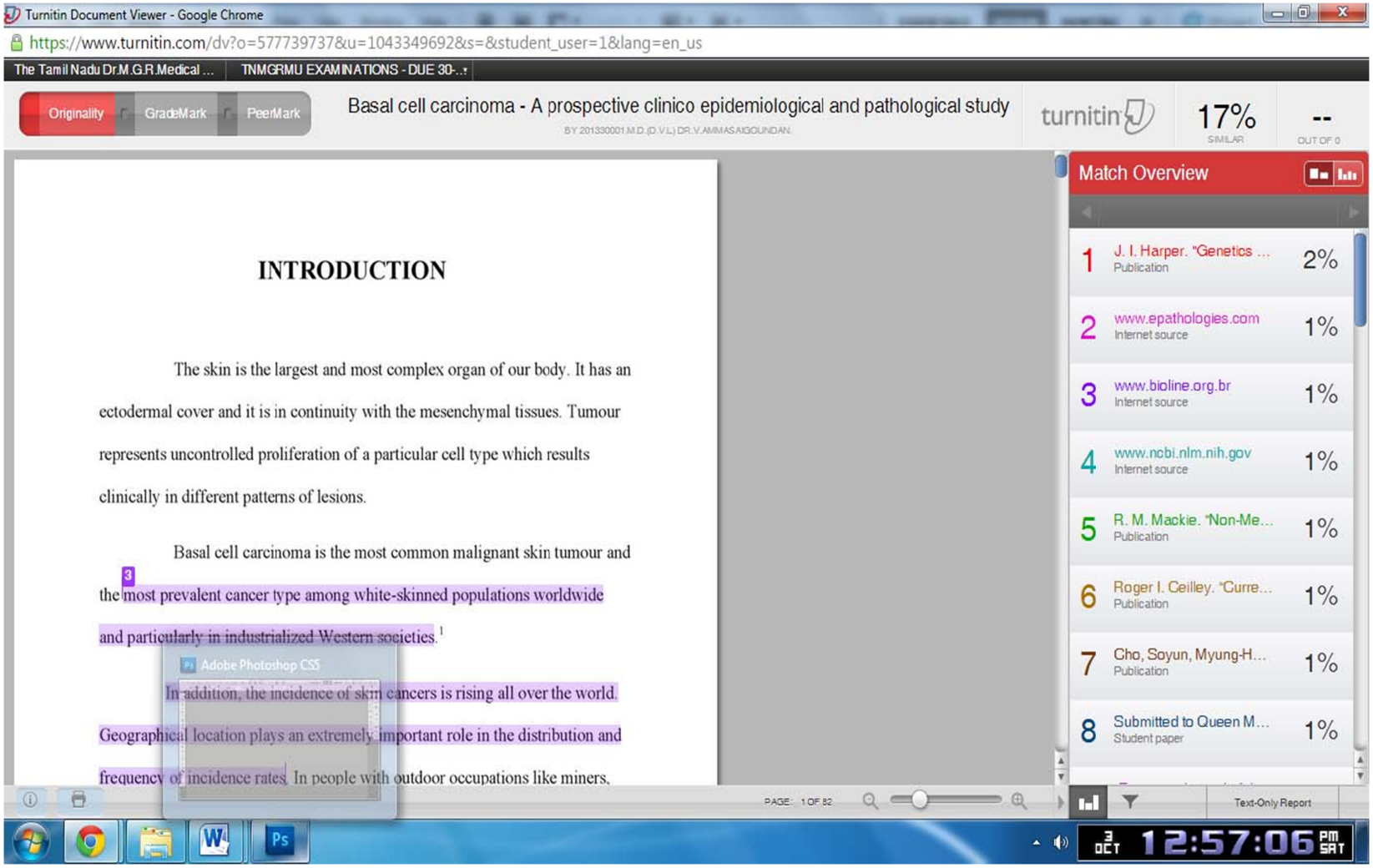
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INTRODUCTION
The skin is the largest and most complex organ of our body. It has an ectodermal cover and it is in continuity with the mesenchymal tissues. Tumour represents uncontrolled proliferation of a particular cell type which results clinically in different patterns of lesions.
Basal cell carcinoma is the most common malignant skin tumour and the most prevalent cancer type among white-skinned populations worldwide and particularly in industrialized Western societies.[1]
In addition, the incidence of skin cancers is rising all over the world. Geographical location plays an extremely important role in the distribution and frequency of incidence rates. In people with outdoor occupations like miners,
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CONTENTS

"BASAL CELL CARCINOMA – A PROSPECTIVE CLINICO EPIDEMIOLOGICAL & PATHOLOGICAL STUDY"

ABSTRACT

AIMS AND OBJECTIVES:

To find out the age and sex incidence of basal cell carcinoma in patients attending the outpatient department of dermatology, RGGGH, Chennai. To find out the various clinical and histopathological features of basal cell carcinoma.

MATERIALS AND METHODS:

This was a prospective observational study carried out at dermatology outpatient department, RGGGH, Chennai. Patients with clinical diagnosis of basal cell carcinoma were included in the study after thorough history, clinical examination, routine and special investigations like skin biopsy.

RESULTS:

Out of 20 patients with basal cell carcinoma 6 were males and 14 were females with a male to female ratio of 1:2.33. Females (70%) were most commonly affected than males (30%). Most commonly affected age group was 50 – 70 years (70%). Distribution of basal cell carcinoma in our study was confined to head and neck area and the most common site involvement was nose (30%), followed by periocular region (25%) and cheek (15%). Most common morphological subtype encountered in our study was nodular / nodulo-ulcerative BCC (70%), followed by pigmented type (25%) and superficial BCC (5%). The most common histological variant observed in our study was nodular

type (55%), followed by pigmented variant (25%), adenoid (5%), basisquamous (5%), superficial BCC (5%) and BCC with sebaceous differentiation (5%).

CONCLUSION:

- This study highlights a paradoxically increasing trend of BCC with female predilection.
- Since early age of onset of basal cell carcinoma being reported in persons with genetic defect, these patients should be advised for periodic follow-up and strict photo protective measures.
- Early detection and treatment of lesions are crucial to decrease the functional and cosmetic morbidity, this study highlights the importance of improving awareness among general practitioners, public health workers and general population.

KEY WORDS:

Basal cell carcinoma, clinical variants, exicision biopsy, histopathology.

INTRODUCTION

The skin is the largest and most complex organ of our body. It has an ectodermal cover and it is in continuity with the mesenchymal tissues. Tumour represents uncontrolled proliferation of a particular cell type which results clinically in different patterns of lesions.

Basal cell carcinoma is the most common malignant skin tumour and the most prevalent cancer type among white-skinned populations worldwide and particularly in industrialized Western societies.[1]

In addition, the incidence of skin cancers is rising all over the world. Geographical location plays an extremely important role in the distribution and frequency of incidence rates. In people with outdoor occupations like miners, quarry men, railway engine drivers and firemen, the frequency of BCC is high.[2]

It is a slow-growing malignant tumour of the skin that invades the adjacent tissues with a metastatic incidence of 0.01% - 0.028%.[3]

Ultraviolet radiation plays a major role in the development of BCCs. Radiation exposure, exposure to arsenic salts, chemical carcinogens, chronic irritation, chronic inflammation, pre existing skin

lesions such as discoid lupus erythematosus, burn scar and vaccination scar are the various other causal factors.[4]

Immunosuppression also to be suspected a role in the pathogenesis of skin cancer. Incidence basal cell carcinoma is high among immunosuppressed individuals and the lesions were commonly found on trunk and arms as compared to immunocompetant patients.

Ethnical differences in types of skin, immunological and genetic factors also play a role in the development of BCC.

Head and neck are known as the most common localizations of basal cell carcinoma (80%), but the anatomical site distribution is different for the histological subtypes. Head and neck is the most common site for nodular BCC whereas the trunk is the most common location of superficial BCC.[5]

Males are most commonly affected than females. A population based incidence survey in Australia shows an annual incidence of 849 in males and 605 in females per100000 population.[6]

BCC generally occurs in adults over 40 years of age but it may occur in children and young adults.[7]

In children it is usually associated with genetic defects such as xeroderma pigmentosum, nevus sebaceous, nevoid basal cell syndrome, rombo syndrome or bazex syndrome.

Clinical types:

There are five clinical types basal cell carcinoma known to occur:

1. Nodular basal cell carcinoma
2. Micronodular basal cell carcinoma
3. Superficial basal cell carcinoma
4. Infiltrating / Morpheic basal cell carcinoma
5. Fibroepithelioma of pinkus

Syndromes associated with BCC:

1. Bazex syndrome
2. Nevoid basal cell carcinoma syndrome
3. Linear unilateral basal cell nevus
4. Xeroderma pigmentosum
5. Rasmussen syndrome
6. Rombo syndrome

From histologic point of view basal cell carcinoma can be divided into 2 types:

- Undifferentiated
- Differentiated

Those latter group shows some degree of differentiation towards the cutaneous appendages of hair, sebaceous glands, apocrine glands or eccrine glands.

Undifferentiated BCCs:

1. Nodular BCC
2. Micronodular BCC
3. Pigmented BCC
4. Superficial BCC
5. Morpheic BCC
6. Fibroepithelioma of pinkus

Differentiated BCCs:

1. Keratotic BCC
2. Cystic BCC
3. Adenoid BCC

Histologic variants of basal cell carcinoma:

1. Adamantinoid type
2. Granular type
3. Clear cell type
4. Matricial type

The aim of this study is to estimate the age and sex-related incidence of basal cell carcinoma in our hospital between October 2014 and September 2015 and to classify basal cell carcinoma subtypes according to their location, morphology and histopathological features.

It is confined to the patients attending the Dermatology department, RAJIV GANDHI GOVERNMENT GENERAL HOSPITAL, CHENNAI.

Review of Literature

REVIEW OF LITERATURE

BASAL CELL CARCINOMA

Synonym: Rodent ulcer, Jacob's ulcer, Basalioma

Basal cell carcinoma was first described by Jacob in 1827. Krompecher in 1903 discovered that the tumour was arising from the basal cells of the epidermis.

In 1914, Adamson stated that these are nevoid tumours originating from latent embryonic foci arised from their dormant state at a later period of life, either from embryonic pilosebaceous follicles, or from embryonic sweat ducts. Mallory suggested that they are carcinomas of hair matrix cells.

Foot in 1947 reported that they are carcinomas arising from distorted primordial adnexal-hair, sebaceous or sweat gland.[8]

Wallace and Halpert in 1950, described them as benign tumours of the hair matrix, differentiated to the hair follicle and called them trachoma.[9]

According to Lever they were nevoid tumours or hamartomas arising from the primary germ cells.

DEFINITION:

Basal cell carcinoma is the most common malignant tumour of the skin that usually arising from basal cells of the epidermis and its appendages.[10]

EPIDEMIOLOGY:

Worldwide, white skinned populations have higher incidence of basal cell carcinoma and overall the incidence of BCC is in rising trend. Its incidence rate varies according to ethnicity and geographical location.[1]

Prevalence of this tumour rises within a population as exposure to sunlight increases but the distribution of the lesions does not correlate with the area of maximum exposure to UV rays.[11]

Basal cell carcinomas are commonly seen on sun exposed areas especially on head and neck area.[5] It may also occurs on the trunk, limbs and rarely on palms, soles, mucous membrane & genitals has been reported.[12]

BCC most frequently affects males than females due to greater occupational and recreational exposure to ultraviolet radiation.

Basal cell carcinoma generally occurs in persons older than 40 years of age but it may occurs in children and young adults. There are three rare forms of basal cell carcinoma with early onset.

1. Linear, unilateral basal cell nevus- all lesions are present at birth
2. Nevoid basal cell syndrome
3. Bazex syndrome

In the above last two conditions patients manifest lesions before puberty.[13]

ETIOLOGY & PATHOGENESIS:

1. ULTRAVIOLET RADIATION:

UVB- induced mutations in the keratinocyte cellular DNA initiates tumour formation after a latent period of 20–50 years.

Absorption of UVB by DNA causes photoproducts formation such as cyclopyrimidine dimers and pyrimidine-pyrimidine photoproducts.[14]

These photoproducts cause cytosine–thymidine (C–T) transition. This step is followed by due to failure of the repair mechanism, leading to dysregulation of gene function and tumour formation.

The genes affected by this C–T transition:

1. *ras* proto-oncogene- responsible for cell signaling for many growth factor receptors.
2. *p53* tumor suppressor gene.[15]
3. Drosophila *PTCH1* gene- implicated in the nevoid BCC syndrome.[16]

UVB initiates BCC formation and promotes tumour growth by producing immunosuppression. This is achieved by depletion of Langerhans cells that stimulates cytokines like TNF-α and IL-10 and suppressing helper T cells with a relative increase in suppressor T cells.[17]

Carcinogenic effects of UVA differs from UVB that UVA induces oxidation of adenine base leading to the formation of adenine N-1 oxide and transversion of thymidine to guanine.[18]

Since the UVB dose is high in higher altitude and lower latitude risk of BCC increases in those areas. Intermittent, intense and infrequent sun exposure plays an important role in tumour formation in BCC than total cumulative dosage of UV radiation.[19] Also the teenage period exposure and use of artificial tanning devices are increases the risk of BCC.[20]

2. IONIZING RADIATION:

BCC may be precipitated by exposure to x-ray and grenz ray.[21]

3. ARSENIC EXPOSURE:

Arsenic exposure in the form of either medicinal, occupational or dietary may precipitate the basal cell carcinoma.[22]

4. IMMUNOSUPPRESSION:

There is an association between BCC with HIV infection and organ transplant patients.[23]

When compared to general population, BCC is 11.5 times more common in HIV infected individuals than the general population.[24]

5. OCCUPATIONAL CAUSES:

Occupational exposure to hazardous air pollutants, ionizing radiation and burns may precipitate BCC.

A multicentre European study showed that the frequency of BCCs was higher among miners, quarrymen, railway engine drivers and firemen.[2]

6. OTHER CAUSES:

Occurance of BCC over burn scars [25] and vaccination scars [26] also been reported.

There is evidence of BCC in identical twins has been reported.[27]

BCC known to occur in nevus sebaceous and other adnexal hamartomas.

7. GENETIC FACTORS:

There is an evidence that genetic factors play a role in the susceptibility of some individuals to basal cell carcinoma.[28]

Mutations in the patched homologue 1 gene (*PTCH1*), which is responsible for the nevoid basal cell carcinoma syndrome and some sporadic cases of basal cell carcinoma.[16]

PTCH1 gene mutations attributed to 30–40% of sporadic basal cell carcinomas.

Mutations in the *PTCH1* gene, the receptor of the sonic hedgehog, have downstream effects leading to the accumulation of the transcription factor Gli-1, which may play a role in the development of basal cell carcinomas.[29]

A downstream target of the sonic hedgehog pathway SOX9, which is expressed in all basal cell carcinomas as well as in adnexal neoplasms of the skin. This suggests a possible contribution of SOX9 to the pathogenesis of basal cell carcinomas.[28]

BMI-1, a gene belonging to the polycomb group of epigenetic gene silencers and which is up-regulated by genes in the sonic hedgehog pathway, is overexpressed in basal cell carcinomas.

Various chemokines may contribute to tumour progression. There is also an association with HLA-DR7 and HLA-DR4 in some populations.

Mutations in the *BAX* gene and *P53* gene have also been found in sporadic cases.[30]

CLINICAL FEATURES:

Basal cell carcinoma most commonly occurs over the head, neck, and upper back. Covered sites involvement including the nipple, penis, scrotum, vulva, and perianal region has been reported.[31]

CLINICAL TYPES:

1. Nodular / Nodulo-ulcerative BCC
2. Micronodular BCC
3. Pigmented BCC
4. Superficial BCC
5. Morpheaform BCC
6. Fibroepithelial BCC

1. NODULAR / NODULO-ULCERATIVE BCC:

Nodular BCC is the commonest morphological type (60%–80% of BCC). It is characterized by a pearly waxy papule(s) with central depression, a rolled out or thready translucent border with surface changes include erosion or ulceration, bleeding, crusting may be present.

It slowly ulcerates and infiltrates deeply, causing destruction of the eye and nose and may invade the skull and meninges.

Noduloulcerative basal cell carcinoma, pigmented

2. MICRONODULAR BCC:

The lesions are flat to raised with poorly defined clinical margins. It may have diffuse infiltrative growth pattern that extends beyond the clinically apparent margins of the tumour. This type has been associated with a higher rate of local recurrence than other types.

Micronodular basal cell carcinoma

3. PIGMENTED BCC:

The morphology of pigmented BCC resembles those of nodular type, the only difference is that the pigmented type shows brown pigmentation of the lesion due to proliferation of melanocytes in the tumour.

4. SUPERFICIAL BCC:

It forms 10-30% of basal cell carcinomas. It consists of erythematous, scaly, slightly infiltrated patches that slowly increase in size by peripheral extension. These patches are surrounded by a fine, threadlike, pearly border.

Some small areas of patches usually show superficial ulceration and crusting. In addition, their centre may show smooth, atrophic scarring.

In contrast to the first three types of basal cell carcinoma, which are commonly situated on the face, superficial BCC mostly occurs on the trunk.

Superficial basal cell carcinoma

5. MORPHEAFORM BCC:

This present as a solitary, flat to depressed, scar like, whitish to yellowish indurated plaque with indistinct borders. The surface is smooth and shiny. The overlying skin remains intact for a long time before ulceration finally occurs.

The term morpheaform arises from a clinical resemblance to localized scleroderma or morphea. In this type the tumours, despite being deeply infiltrative, may be mistaken clinically for a lesion of morphea or for a scar.

Morpheic type of basal cell carcinoma

6. FIBROEPITHELIAL BCC:

It manifest as solitary to multiple, sessile to pedunculated, firm nodules covered by smooth, slightly reddened skin. Clinically they resemble fibromas. The most common location is on the back, especially in the lumbosacral region. Prior radiotherapy is a predisposing factor. The course of this type is indolent, however invasion may occur.

SYNDROMES ASSOCIATED WITH BCC:

There are certain clinical syndromes in which basal cell carcinoma occurs more frequently, at an early age and with environmental factors either playing a role or facilitating tumour formation.

1. Bazex syndrome:

It was first described in 1966.[32] It is an autosomal dominant inherited condition showing follicular atrophoderma.

It is characterized by widened follicular openings, like ice pick marks, mainly on the extremities and multiple, small, basal cell carcinoma on the face. It is common in the childhood, adolescence or early adulthood.[33]

In addition, localized anhidrosis, generalized hypohidrosis and congenital hypotrichosis on the scalp, as well as in other areas is also seen.

2. Nevoid basal cell carcinoma syndrome:

(Gorlin syndrome)

In 1963, Gorlin described this syndrome. It is an autosomal dominant condition, characterized by multiple basal cell carcinomas occurring all over the body, predominantly over exposed sites and usually manifest between 2-35 years of age.

Started as small nodules and during the “nevoid” stage, there is increase in the number and size of the nodules and distributed over the face and body.

During adulthood, many of the BCCs undergo ulceration and in later life, the disease enters into a “neoplastic” stage in which some of the basal cell carcinomas, especially facial lesions become invasive, destructive, and mutilating.

Occasionally, even death may result from invasion of an orbit and of the brain. There also may be metastases to the lung.[34]

It is associated with milia, epidermal cysts, abnormal ribs, dental cysts, characteristic facies and scoliosis, kyphosis, short metacarpals, keratosis of palms and soles, supernumery digits, agenesis of corpus callosum, dural and periventricular calcification, ovarian fibromata, hypogonadism, cataract, mental deficiency, congenital hydrocephalus and occasional cerebellar medulloblastomas and calcium deposits in the skin. Rarely fibro sarcoma of the mandible[35] and ameloblastoma of the lower jaw may occur**.**

One of the hallmarks of this syndrome is numerous superficial pit like depression of the palms and soles 1-3mm in diameter, commonly occurring in the 2nd decade of life or afterwards and they represent forme frusta of basal cell carcinoma.

3. Linear unilateral basal cell nevus:

It is a rare condition, which is characterized by extensive unilateral linear or zosteriform eruption, usually present since birth, consisting of closely set nodules of basal cell carcinoma.[36] The lesions may be interspersed with comedones [37] and striae-like areas of atrophy [38]. They do not increase in size with aging of the patient.

4. Xerodermo pigmentosum:

Definition:

Xeroderma pigmentosum (XP) is an autosomal recessive disease characterized by photosensitivity, pigmentary changes like oculocutaneous pigmentation, premature skin ageing and early neoplasia resulting from abnormal DNA repair. Some XP patients have neurological complications.[10]

Pathogenesis:

Pathogenesis of xeroderma pigmentosum involves there is defect in the nucleotide-excision-repair (NER) pathway, responsible for the removal and replacement of damaged DNA.[39]

This results in diminished DNA repair in the cells exposed to the UVB range of sunlight(290-320nm). This explains the photosensitivity and carcinogenesis observed.

Xeroderma pigmentosum and neoplasia:

In XP patients, Cultured dermal fibroblasts exhibit increased UV-induced mutagenesis. This results in neoplasms in XP patients, which occur predominantly on sun-exposed surfaces, are thought to be the result of UV-induced mutations.[40]

Even though skin tumours from xeroderma pigmentosum patients carry mutations bearing a 'UV signature' in the *p53* and *PTCH* genes.[41] UV exposure also triggers a complex series of signal transduction pathways that result in immunosuppression of the skin.[42] This may also be an important factor in patients with XP.

Clinical features:

Xeroderma pigmentosum is a multi-system disorder involving the skin, eyes, and nervous system. The patients have poor physical development and short stature. The affected children may be normal at birth.

Cutaneous features are persistent erythema, acute sun-burn, xerosis and diffuse freckling usually involve photo-exposed body parts by the age of 6 months to 3 years. The freckles are varying in colour light to dark brown, pinpoint to 1 cm in size, progressive, and permanent.

Freckles first appear on the face and hands and later on other exposed parts, the neck and lower legs, lips and conjunctiva. In severe cases the trunk also affected and keratoacanthoma are common in XP.

There may be associated small, round, white atrophic macules giving rise to a mottled appearance. As they progressively increase in

number, telangiectases and small angiomas appear interspersed among them.

Most of the cases when manifest in early childhood reach the tumour stage before the age of 20 years. Premalignant conditions like actinic keratoses and keratoacanthoma are common in XP.

Basal cell carcinoma may develop as early as in the third or fourth year of life in patients with XP. Here BCCs are multiple, mostly of the pigmented variety. Other malignancies like squamous cell carcinoma and malignant melanoma also common, that may be multiple and co-occurrence of these tumors may occur. Mutilation of facial features may resulting from malignant tumours.

Ocular manifestations include photophobia, conjunctival xerosis, and recurrent conjunctivitis are present in 80% patients with xeroderma pigmentosum (XP1) in the initial months of life. Freckle-like pigmented macules gradually appear in the bulbar conjunctiva. Scarring of the eyelids, loss of eyelashes, symblepharon, and ectropion may result from acute episodes of photo damage. Other ocular changes include vascular pterygium, corneal opacities, ocular keratoacanthoma, and epithelioma of the eyelids.

Neurological abnormalities are present in approximately 20% of the patients with XP1. These start manifesting in early infancy, up to the second decade. The clinical features include mental retardation, areflexia/hyporeflexia, spasticity, ataxia, and sensorineural deafness occurring in varying combination.

Neurological involvement is thought to arise from accumulation of DNA damage in the absence of adequate nucleotide-excision-repair (NER), ultimately leading to neuronal death.

5. Rasmussen syndrome:[43]

It is a syndrome of trichoepithelioma, milia, and cylindromas. Autosomal dominant pattern of inheritance. Histopathologically, the trichoepitheliomas and milia contained keratinizing cysts with laminated centers, peripheral basaloid cells and a thin granular layer.

6. Rombo syndrome:[44]

It is a rare genetic disorder characterized mainly by atrophoderma vermiculatum of the face, multiple milia, hypotrichosis, telengiectases, acral erythema, trichoepithelioma, basal cell carcinoma and peripheral vasodilatation with cyanosis.

The lesions become visible in late childhood, begins at ages 7 to 10 years and most pronounced on face.

BOILOGIC BEHAVIOUR:

Local invasion:

The dangerous consequences of BCC results from local invasion. In general, basal cell carcinoma is a slow-developing malignant tumour have an aggressive behaviour with local tissue invasion and destruction.[45]

Metastases are rare and it is closely correlate to the size and depth of tumour invasion and less so to the histological subtype of the original tumor.[4]

Although metastases are rare, significant morbidity, such as local tissue destruction and disfigurement can occur. There is a case report of giant BCC in India, a patient presented with a nonhealing ulcer of the face, which is increasing in size for over 20 years. On examination, the ulcer covered the entire left side of the face involving the preauricular, infraorbital, and bucco mandibular units of the cheek and the orbit and resulted in loss of vision.[46]

Perineural invasion:

Perineural invasion (PNI) mostly occurs in recurrent and histologically aggressive BCCs.[47] The presence of PNI has been correlated with recurrent lesions, increased duration and size of lesions and orbital invasion.[48]

A study by Niazi and Lamberty observed that PNI in < 0.2% of cases and perineural BCC was reported in recurrent tumours with preauricular and malar areas in location.[49]

Perineural spread in cases of periocular BCCs may results in orbital invasion. It may require extensive surgery and exenteration.[50]

METASTASIS:

Metastasis of basal cell carcinoma is rare, with an incidence of metastasis ranging from 0.01% to 0.028%.[3] Metastasis to regional lymph nodes and lungs is most common.[51] Metastasis to the bone and bone marrow also been reported.[52]

Risk factors for metastasis:

1. Large size of the primary tumour (Giant BCC- >10 cm)
2. Long standing lesion
3. Recurrent tumour
4. Aggressive histological pattern - morpheic, infiltrating and micronodular types of BCC
5. Perineural invasion

HISTOPATHOLOGY:

The characteristic cell in BCC is the basalioma cell which has a large oval or elongated nucleus and relatively little cytoplasm. These cells do not reveal any inter-cellular bridges when seen by light microscope. The nuclei of the basilioma cells are uniform in size and uniformly stained as well.

The connective tissue stroma is arranged in parallel bundles around the tumour masses.The stroma appears mucinous and reacts metachromatically. There are retraction clefts seen around the tumour masses and lacunae are present due to the absence of the bullous pemphigoid antigen.[53]

A mild inflammatory infiltrate may be seen, but dense lymphocytic infiltrate is usually seen if the lesion clinically shows ulceration. In addition, there are variable degrees of cytologic atypia and mitotic activity.[54]

From the histological point of view basal cell carcinoma divided into 2 groups:

1. Undifferentiated
2. Differentiated

Undifferentiated BCCs:

1. Nodular BCC
2. Micronodular BCC
3. Pigmented BCC
4. Superficial BCC
5. Morpheic BCC
6. Fibroepithelioma of pinkus

Differentiated BCCs:

1. Keratotic BCC
2. Cystic BCC
3. Adenoid BCC

Histologic variants of basal cell carcinoma:

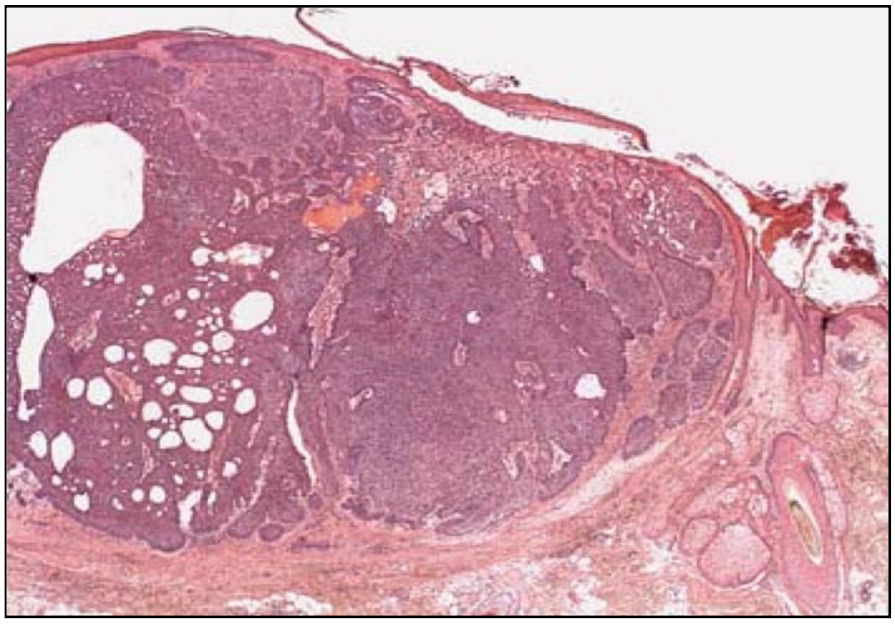
1. Adamantinoid type
2. Granular type
3. Clear cell type
4. Matricial type

Undifferentiated BCCs:

1. Nodular basal cell carcinoma:

It consists of nodules of basaloid cells with a peripheral palisade arrangement. Each basaloid cell having a large, oval, and elongated nucleus and scanty cytoplasm. The nuclei of basal cells are uniform and nonanaplastic and no variation in staining properties or abnormal mitoses.

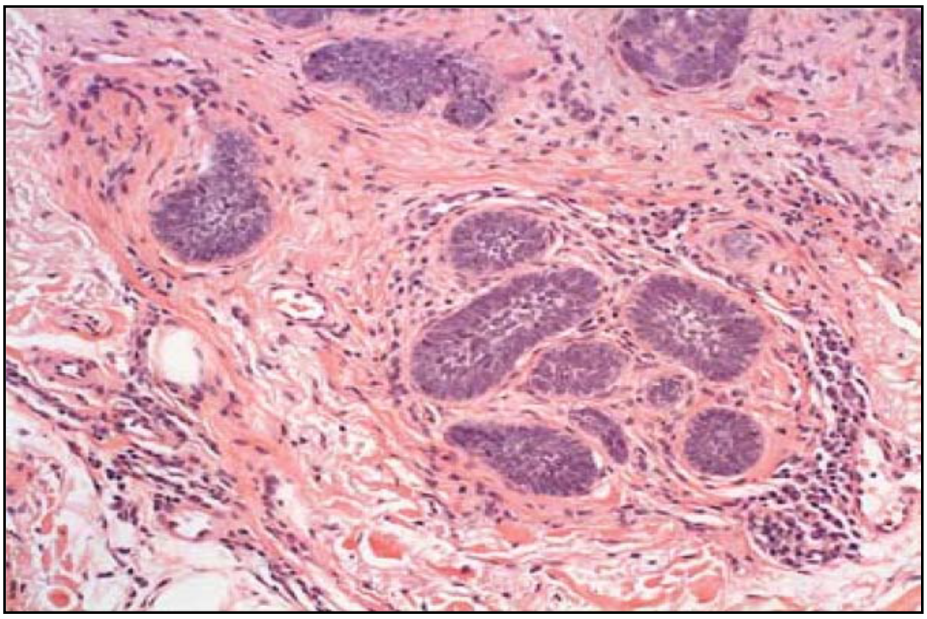
Large cystic spaces are formed within the tumour masses due to tumour cell degeneration. Retraction artefacts may be present around the tumour nodules. In connective tissue stroma the nodules are arranged as parallel bundles around the tumour islands and there may be mucinous or amyloid deposits. In nodular BCC, the dermal infiltrate is mild to moderate, but it becomes dense if ulceration occurs.



Nodular type of basal cell carcinoma

2. Micronodular BCC:

It consists of small nodules in the upper dermis. It is the least common type but it carries high risk of local recurrence. They vary between symmetric, circumscribed to asymmetric and infiltrate between collagen bundles.

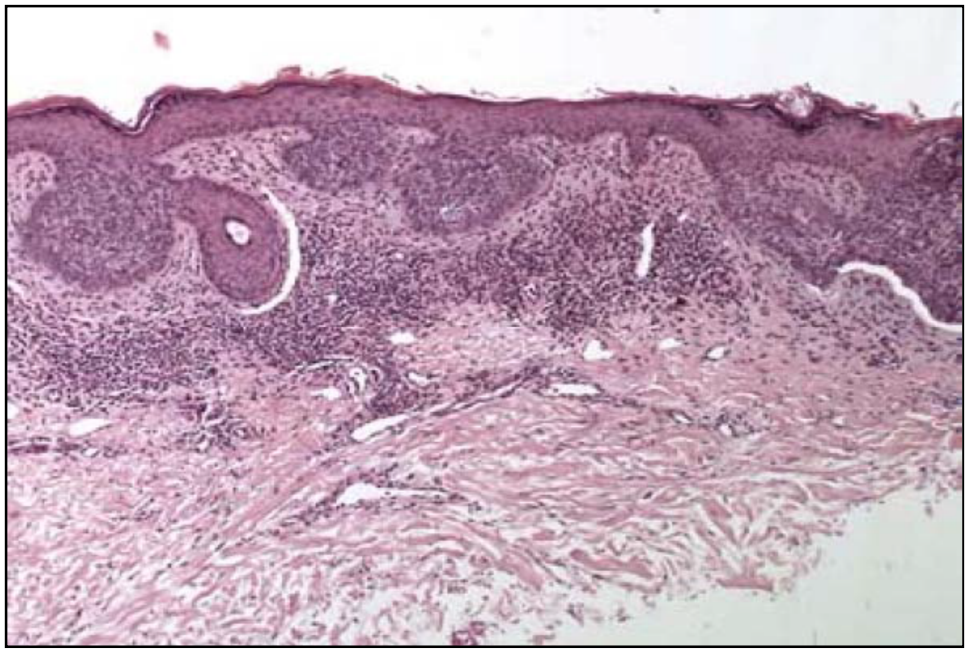


Micronodular basal cell carcinoma

The tumour may infiltrate deeply into the dermis to involve the excision margin. Micro-nodular differentiation is seen typically towards the base of a tumour. There is an overlap of appearances between micronodular and morpheic type of basal cell carcinomas.

3. Superficial BCC:

There is budding and irregular proliferation of malignant cells extends from the basal layer of the epidermis into the dermis.[55] The islands of tumor mass may attach to the under surface of the epidermis, hair follicles or eccrine ducts. The peripheral cell layer of the tumor shows palisading. There is only minimal invasion into papillary dermis. The tumor islands are surrounded by fibroblasts and there may be inflammatory infiltrate in the upper dermis.

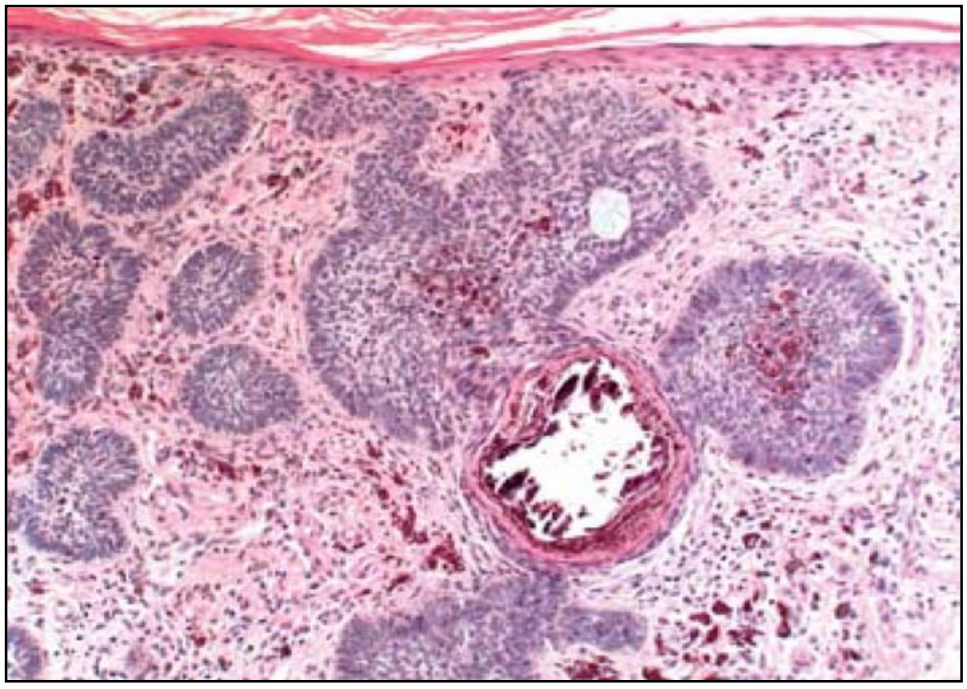


Superficial basal cell carcinoma.

The tumor shows buds and irregular proliferation of tumor tissue attached to the under surface of the epidermis.

4. Pigmented BCC:

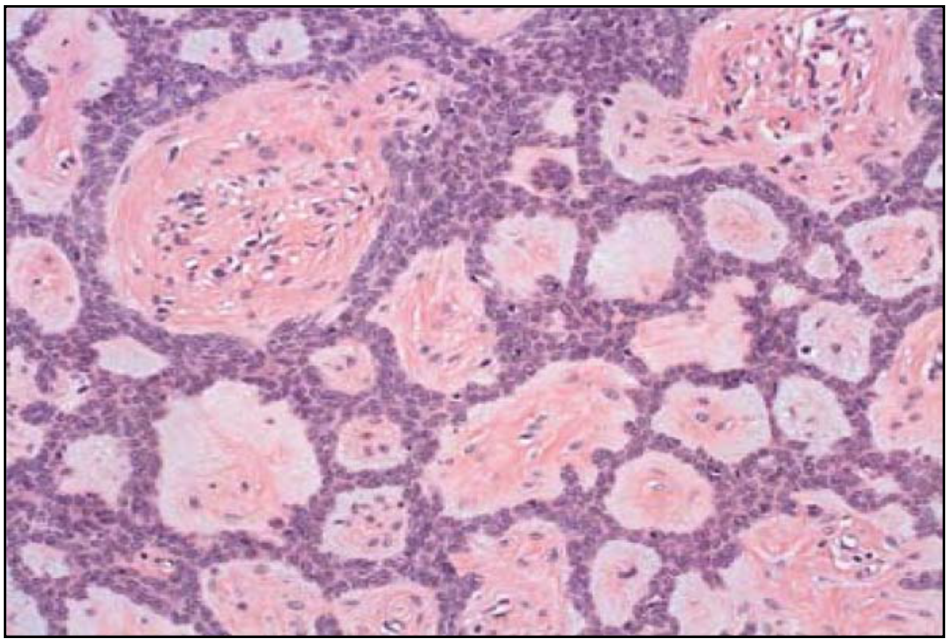
Histological features of pigmented BCC is resembles with nodular BCC. In addition melanin pigment is present within solid islands of basal cell carcinoma and in macrophages between the islands of tumor cells. Melanocytes are present approximately in 75% of BCCs and melanin content of BCC is about 25%. The melanocytes contains plenty of melanin granules in their cytoplasm and intermingled between the tumor cells. There may be numerous melanophages in the stroma surrounding the tumor.[56]



Pigmented basal cell carcinoma

5. Fibroepithelioma of pinkus:

It was first described by Pinkus in 1953.[57] In this type long, thin, branching, anastomosing strands of basal cell carcinoma are embedded in a fibrous stroma. Many of these strands have connections with the surface epidermis. There are small groups of dark-staining cells showing peripheral palisading along the epithelial strands, like buds on a branch. The tumor is quite superficial and its lower border is well demarcated. Fibroepithelioma can change into an invasive and ulcerating basal cell carcinoma.[58]



Fibroepithelioma of pinkus

Differentiated BCCs:

1. Keratotic type-Differentiation towards hair structures
2. Cystic type-BCC with sebaceous differentiation
3. Adenoid type- Differentiation towards tubular structures

Keratotic type:

This type shows parakeratotic cells and horn cysts in addition to the undifferentiated tumour cells. The parakeratotic cells have an elongated nuclei and eosinophilic cytoplasm – lie in the strands, concentric whorls or around the horn cysts and the latter contain fully keratinized cells and represent attempts of hair shaft formation.

Cystic type:

This type shows cystic spaces within the tumour lobules. The cyst formation is due to necrobiotic changes of tumour cells. The cells in the centre show a vesicular appearance suggesting differentiation into sebaceous cells**.**[59]

Adenoid type:

This type shows tubular or glandular like structures. The cells arranged in intervening strands resulting in a lace like pattern. The lumina are filled with a colloid substance or an amorphous granular material. The

degree of differentiation is low that even with histochemistry, it is not possible to say whether the differentiation is towards apocrine or eccrine glands.[60]

HISTOLOGICAL VARIANTS OF BCC:

There are 4 common histological varients of basal cell carcinoma.

1. Adamantinoid type
2. Granular type
3. Clear cell type
4. Matricial type

Adamantinoid basal cell carcinoma:

Adamantinoid BCC shows a histological resemblance to dental ameloblastoma or adamantinoma.[61] There is solid masses of basaloid cells with palisading at the periphery. Inside this layer, the cells have elongated nuclei and stellate cytoplasm and it is stretched as thin, connecting bridges across empty spaces, as seen in adamantinoma.

Granular BCC:

In granular basal cell carcinoma some of the tumor cells have the usual basaloid cells appearance, whereas others show a gradual transition to granular cells. The granular cells shows eosinophilic granules with a

tendency to coalesce.[62,63] These granule resembles those seen in granular cell tumour.

Clear cell basal cell carcinoma:

In the clear cell BCC the clear cell pattern may occupy all or part of the tumor islands. The clear cells contain vacuoles of varying sizes filled with glycogen.[64] The vacuoles may cause peripheral displacement of the nucleus and giving the cells with signet ring appearance.[65]

Matricial BCC:

In this type there is islands of shadow cells, as seen in pilomatricoma, are located within a basal cell carcinoma.[66]

DIFFERENTIAL DIAGNOSIS:

Nodular BCC:

- Dermatofibroma
- Appentageal tumor
- Squamous cell carcinoma
- Dermal nevus

Morpheic BCC:

- Morphea
- Scar
- Trichoepithelioma

Pigmented BCC:

- Compound nevus
- Lentigo maligna melanoma
- Nodular melanoma
- Blue nevus
- Superficial spreading melanoma

Superficial BCC:

- Extramammary paget's disease
- Superficial spreading melanoma
- Bowen's disease
- Single plaque of eczema
- Single plaque of psoriasis

Fibroepithelioma of pinkus:

- Fibroma
- Skin tag
- Papillomatous dermal nevus

DISEASE STAGING:

The staging of basal cell carcinoma is based on TNM classification, established by the American Joint Committee of Cancer.[67]

TNM classification of basal cell carcinoma:

T	-	Tumour
X	-	Primary cannot be assessed
T0	-	No evidence of primary tumour
T1	-	Tumour <2 cm in size with <2 high risk features
T2	-	Tumour >2 cm in size, tumour of any size with high risk features (>2 mm breshlow thickness, perineural invasion, ear as primary site, undifferentiated carcinoma)
T3	-	Tumour with invasion of maxilla,mandible,orbit or temporal bone
T4	-	Tumour with invasion of skeleton or perineural invasion of skull base
N	-	Lymphnode
X	-	Lymphnode cannot be assessed
N0	-	No regional lymphnode metastasis
N1	-	Metastasis in a single ipsilateral lymphnode <3 cm in size

N2 - Metastasis in a single ipsilaterl lymphnode >3 cm but <6cm in size or multiple ipsilaterl lymphnodes <6 cm in size or bilateral / contralateral lymphnodes <6 cm in size

N3 - Metastasis in a lymphnode >6 cm in size

M - Metastasis

X - Metastasis cannot be assessed

M0 - No distant metastasis

M1 - Distant metastasis

Patients with a primary cutaneous basal cell carcinoma with or without evidence of regional or distant metastases are divided into the following stages:

Stage 1 : Tumor is 2 cm or less in size, no metastasis

Stage 2 : Tumor is more than 2 cm in size, no metastasis

Stage 3 : Any size of the tumor with one lymphnode involvement measuring 3 cm or less in size or extension of tumor into the maxilla, mandible, orbit or temporal bone

Stage 4 : Patients with tumor with direct or perineural invasion of skull base or those with two or more lymphnodes involvement and distant metastasis.

TREATMENT:

The choice of therapy depends on the site, the size, the number of lesions. The success of therapy depends on early recognition, accurate histological typing and the method of treatment. The therapy is not satisfactory when the basal cell carcinoma involves the orbit, nose or ear.

METHODS OF TREATMENT:

1. Surgical exicision
2. Mohs' micrographic surgery
3. Cryosurgery with liquid nitrogen.
4. Radiotherapy
5. Combination therapy: Surgery + Irradiation of the lesion.
6. Local cytotoxic therapy
    a. Topical 5% Imiquimod cream
    b. Topical 20% 5-FU ointment
7. Interferon therapy
8. Photodynamic therapy
9. Laser

Surgical exicision:

Surgical excision has the advantage over nonexcisional techniques that histologic confirmation can be made from surgically removed specimen.[68]

A recent Cohrane review concluded that surgical exicision is the best method of treatment for basal cell carcinoma.[69]

Conventional surgical excision with predetermined margins based on the clinical characteristics of the tumour and provides a specimen for histological examination and assessment of the lateral and deep margins yielding <2% recurrence rate at 5 years post surgery.[70]

Margins of surgical exicision 4 mm were adequate for treating nonmorpheaform BCCs < 2 cm in diameter observed by Wolf and Zitelli.[71]

Chiller et al found that preoperative curatage decrease the positive margins and surgical failure rate of BCC by 24%.[72]

Disadvantages:

- Potential for incomplete margin control
- Standard surgical exicision cure rate is low as compared to mohs micrographic surgery for treating recurrent basal cell carcinomas, morpheic BCCs and high risk anatomical location of tumor.[73]

Mohs' micrographic surgery:

- Mohs' micrographic surgery is the treatment of choice for high-risk primary BCCs, morpheaform, poorly delineated, incompletely exicised and recurrent BCCs.
- It is best method for treating BCCs located on high-risk anatomic sites, such as nasolabial fold, periorbital region and postauricular sulcus.
- MMS provides the lowest recurrence rates and it is the first treatment of choice for primary facial BCCs with an aggressive histopathological subtype.[74]
- Mosterd et al also found that treatment with mohs micrographic surgery leads to a significantly lower number of recurrences than treatment with surgical excision in recurrent facial BCCs.[75]

Curettage and desiccation:

- Curettage & desiccation is operator-dependent and most frequently used treatment modalities for BCC.[76]
- For appropriately selected lesions and locations, C&D remains an efficacious and cost-effective treatment modality.

Disadvantages:

- Recurrences were common for lesions located on the nose, temple, forehead and ears.
- It is not recommended for treating morpheic BCC, recurrent BCC and large primary BCC.

Cryosurgery:

- Cryosurgery is a destructive method of treatment that has been used for treating basal cell carcinoma.
- 2 freeze-thaw cycles are required for destruction of BCC at a tissue temperature of −50°C.
- To avoid subclinical extension margin of normal tissue also to be destroyed.

Disadvantages:

- Lack of histological confirmation of tumor removal.

- Complications include post inflammatory hyperpigmentation and hypertrophic scar.[77]
- Another bad outcome is the fibrous scar tissue may hide the tumor recurrence.

TOPICAL TREATMENT:

1. Topical Imiquimod
2. Topical 5-FU

Topical imiquimod:

- FDA approved Imiquimod 5% cream in 2004 for the topical treatment of biopsy confirmed, small (less than 2 cm), primary superficial BCC.
- Imiquimod is an immuno modulator acts as Toll-like receptor- 7 agonist there by induce T helper immunity by stimulating interferon-α, tumor necrosis factor-α, and other cytokines .
- Possible adverse effects include local skin reactions-erythema, erosion and crusting.

Topical 5-fluorouracil:

- 5-FU can be used topically to treat basal cell carcinomas.
- It should be applied at bed time over the lesion including 1 cm of skin surrounding the tumor, 5 days a week for 6 weeks.

- Gross et al reported a 90% histologic clearance rate after 3 weeks of topical 5-FU treatment.[78]
- 5-FU is generally well tolerated with a good cosmetic outcome and with only minimal side effects like mild erythema.
- 5-FU is contraindicated in dihydropyrimidine dehydrogenase enzyme deficient patients.

Interferon therapy:

- Interferon α-2b has also been tried in a schedule of 1.5 million units injected intralesionally 3 times per week for a period of 3 weeks.

Photodynamic therapy (PDT):

- Mechanism of PDT involves visible light activates photosensitizing drug there by producing activated O_2 species that destroy the cancer cells.
- Use of photosensitizers like 5-aminolevulinic acid is followed by irradiation with light sources like tungsten filament, xenon arc, metal halide, and fluorescent lamps, or lasers like the dye, metal vapor, Nd:YAG, light-emitting diode and femtosecond lasers. This leads to mean clearance rates of 87% in superficial BCC and 53%–71% in nodular BCC with a recurrence rate of 0%–31%.

- It is useful for superficial tumors (tumor thickness <3 mm), simultaneous treatment of multiple tumors and in immunocompromised patients.
- In extensive BCCs it is used a adjuvant to Mohs micrographic surgery. It has the advandage of short healing time and excellent cosmetic result.
- Cure rates for superficial BCCs with Photodynamic therpy is around 75% and patients should be monitored closely during the first 2–3 years after PDT.

Radiation therapy:

- It is usefull for a patient unwilling or unable to undergo surgery.
- X-ray therapy may be a very useful modality as adjuvant treatment for BCC when margins are positive after excision or for extensive perineural or large nerve involvement.[79]

Disadvantages:

- Lack of histologic confirmation of tumor removal,
- Prolonged treatment course
- Worsening of cosmetic outcome over time like cutaneous atrophy and telangiectasia.

- It may predispose to aggressive and extensive recurrences.
- The Cochrane Collaboration found surgery and radiotherapy to appear the most effective treatments for BCC.[80]

Lasers:

- Co2, Nd:YAG and photo dynamic lasers can be used to ablate the lesion.

COURSE AND PROGNOSIS:

- Prognosis of BCC is better with appropriate treatment.
- Mohs' micrographic surgery yields better control rates as high as 99%.
- Monitoring is required for recurrence and development of new primary BCCs.
- Risk of development of new primary BCC is 36% - 50%.[81]
- Regular follow up and counselling about photo protective measures are required for patients with history of BCC.
- Frequent monitoring is required for patients with recurrence.
- About 40%–50% of patients with primary carcinoma will develop further BCCs within 5 years.
- Prognosis is poor for patients with metastasis.

Poor prognostic factors:

1. Tumour size more than 2 cm
2. Location of the tumour – midfacial distribution
3. Lesions with ill defined margins
4. Immunosuppressed patient
5. Recurrent disease
6. Histological subtype- morpheic / infiltrative,micronodular
7. Aggressive histological features- perineural or vascular invasion

BASISQUAMOUS CARCINOMA:

Basosquamous carcinoma is an aggressive growth form of BCC. It can be confused with squamous cell carcinoma.

Its histomorphologic classification is controversy as it shows both basal cell and squamous cell carcinoma differentiation in a continuous fasion.

Histologically, it shows infiltrating jagged tongues of tumor cells admixed with other areas that shows squamous intercellular bridge formation and cytoplasmic keratinization. In contrast to pure BCC, basisquamous cells lacking classic palisading and exibit cytoplasmic keratinization.

The transition zone may be present between BCC and SCC.

The risk of local recurrence and metastasis is high with basisquamous carcinoma.[82]

Collision tumor:

It is defined as the juxtaposition of two originally separate neoplasms and these are sharply demarcated from each other.

Examples include nevus and basal cell carcinoma, nevus and seborrheic keratosis, squamous cell carcinoma and melanoma.

Aims & Objectives

AIMS & OBJECTIVES

1. To find out the age and sex incidence of basal cell carcinoma in patients attending the out-patient department of dermatology, Rajiv gandhi government general hospital, Chennai.

2. To find out the various clinical presentations of basal cell carcinoma such as morphology, location and size.

3. To find out the histopathological features of the various types.

Materials & Methods

MATERIALS AND METHODS

Study design:

Prospective observational study

Study period:

October 2014 – September 2015

Methodology:

Patients who attend the dermatology outpatient department, Rajiv Gandhi Government General Hospital with a clinical diagnosis of basal cell carcinoma are selected for the study.

Thorough history related to age, sex, occupation and duration of the lesions are noted. Specific and relevant history about the lesion was taken, including family history. History of any medical or surgical interventions are noted.

Thorough clinical examination of the lesions with reference to site, number, size, shape, colour, surface, border and consistency are noted.

Routine investigations like complete blood count, random blood sugar, bleeding time, clotting time, HIV 1&2 antibody, VDRL and X-ray chest are taken for all the patients.

Using pretested proforma, patient details, clinical findings and investigations are recorded.

Exicision biopsy was done at plastic surgery department. Exicised specimen was received for histopathological examination. Sections are stained with H&E and studied in both low & high power magnifications.

Pathologist opinion was obtained. Clinical and histopathological correlation was done.

INCLUSION CRITERIA:

Patients who attend the dermatology outpatient department with clinical diagnosis of basal cell carcinoma.

EXCLUSION CRITERIA:

Patients those who are not willing to participate in the study.

Observation & Results

RESULTS

SEX DISTRIBUTION OF BASAL CELL CARCINOMA:

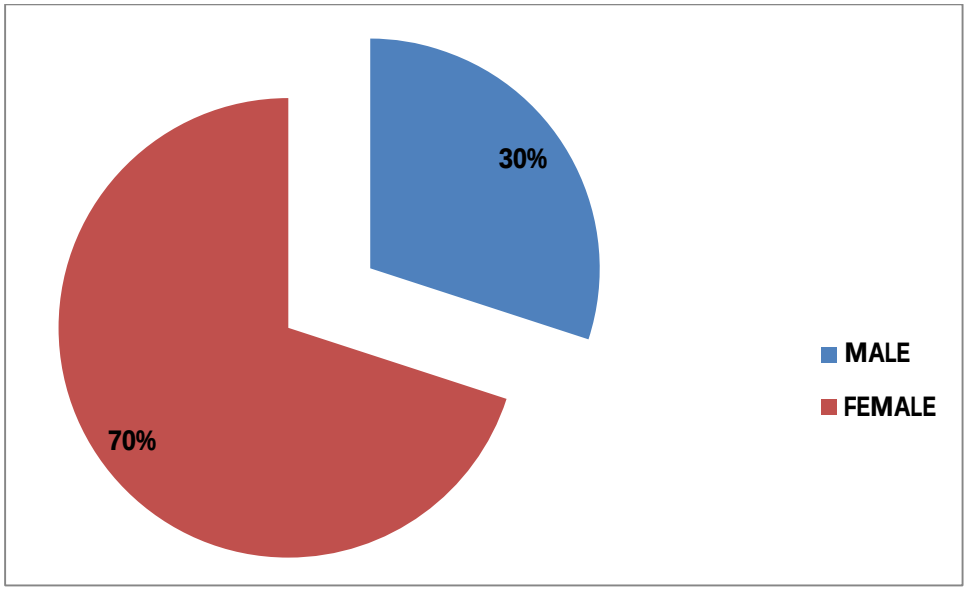
Total of 20 patients with basal cell carcinoma were included in the study. Out of this, 6 patients were males and 14 patients were females.

Hence in our study basal cell carcinoma was more common in females (70%) than males (30%). Male to female distribution was 1: 2.33.

Table 1: SEX DISTRIBUTION (N-20):

MALE	FEMALE
6	14

Figure 1: SEX DISTRIBUTION



AGE DISTRIBUTION OF BCC

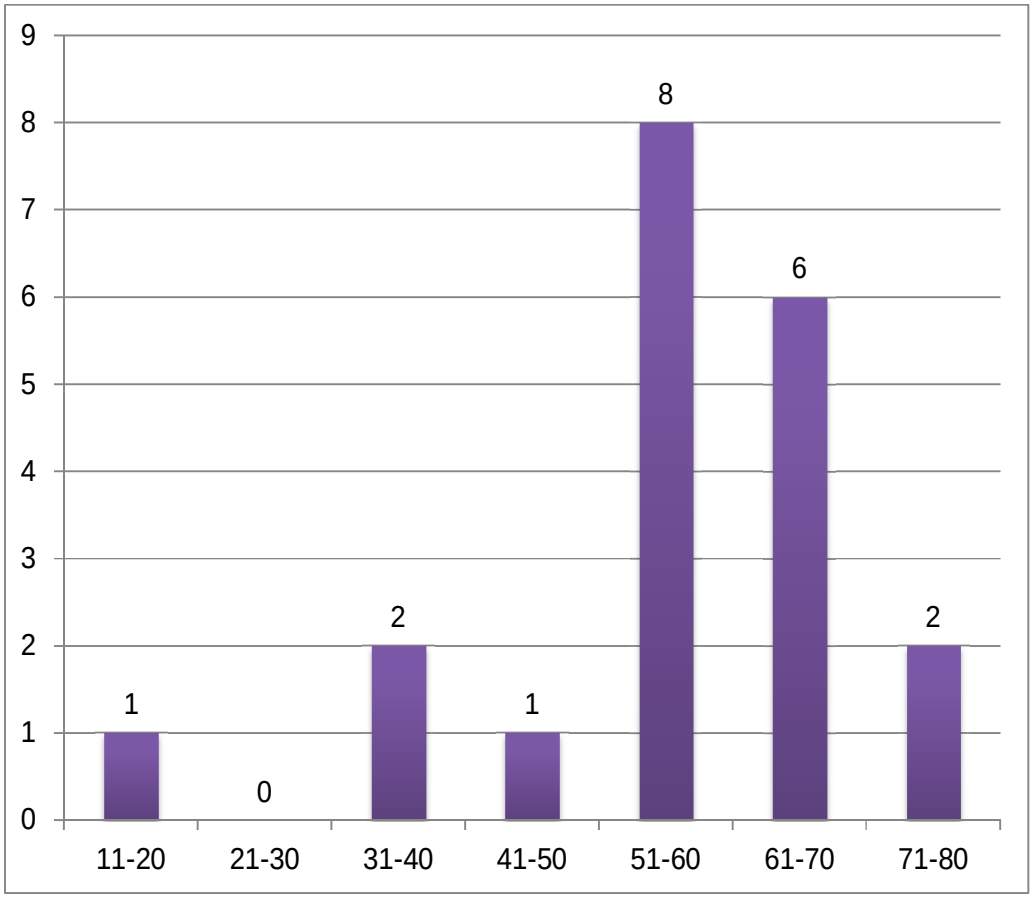
Age of the patients ranged from 10-80 years. The most commonly affected age group was 51-60 years with 8 (40%) patients, closely followed by 61-70 years age group with 6 (30%) patients.

Hence in our study Basal cell carcinoma was most common in the age group of 51-60 years.

Table 2: AGE DISTRIBUTION

AGE	N-20
11 – 20	1
21 – 30	0
31 – 40	2
41 – 50	1
51 – 60	8
61 – 70	6
71 – 80	2

Figure 2: AGE DISTRIBUTION OF BASAL CELL CARCINOMA



Age distribution of basal cell carcinomas were seen more predominantly between 51- 60 years of age with a mean age of 56.7 years.

SEX WISE AGE DISTRIBUTION OF BCC:

In the age group of 51-60 years, there were 8 patients with 2 males and 6 females. It is followed by in the age group 61-70 years there were 6 female patients.

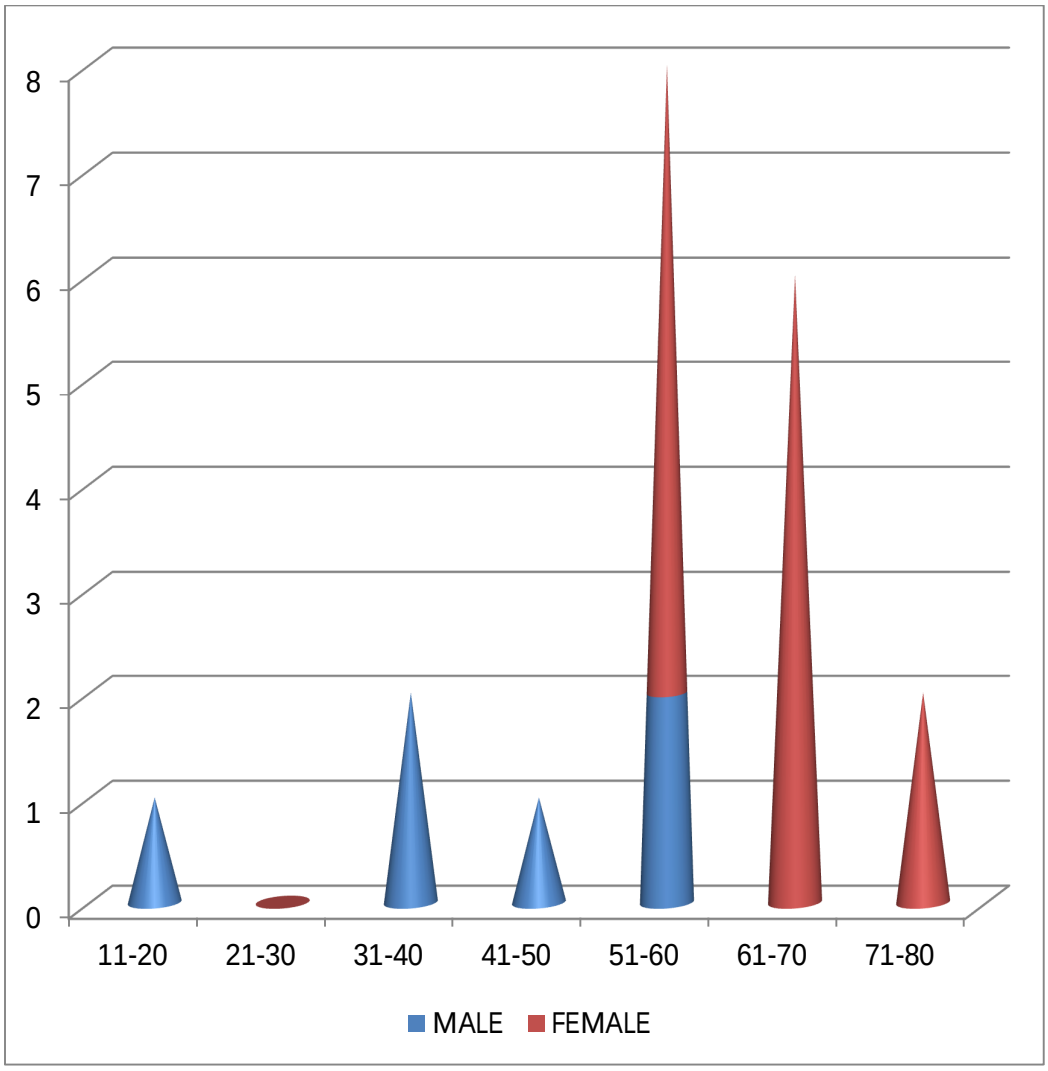
Table 3: SEX WISE AGE DISTRIBUTION OF BCC

Age group	Male	Female	Total	Percentage
11 - 20	1	0	1	5%
21 - 30	0	0	0	0
31 - 40	2	0	2	10%
41 - 50	1	0	1	5%
51 - 60	2	6	8	40%
61 - 70	0	6	6	30%
71 - 80	0	2	2	10%

Males are commonly affected in the age group of 31-40 years (10%) and 51-60 years (10%).

In females most commonly affected age group was noted between 51-60 years (30%) and 61-70 years of age (30%).

Figure 3: SEX WISE AGE DISTRIBUTION OF BCC



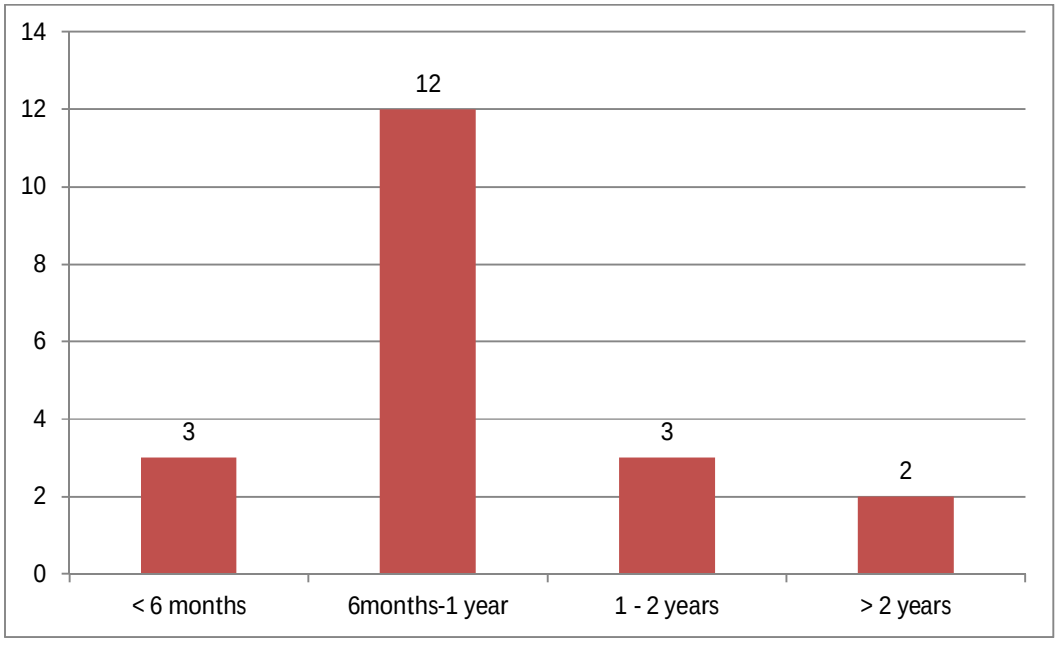
DURATION OF THE DISEASE

12 cases were noted with duration of lesion between 6 months to 1 year. It was followed by 3 cases each were noted with less than 6 months and more than 2 years duration.

Table 4: DURATION OF THE DISEASE

Duration of the lesion	No-20
< 6 months	3
6 months – 1 year	12
1 – 2 years	3
>2 years	2

Figure 4: DURATION OF THE DISEASE



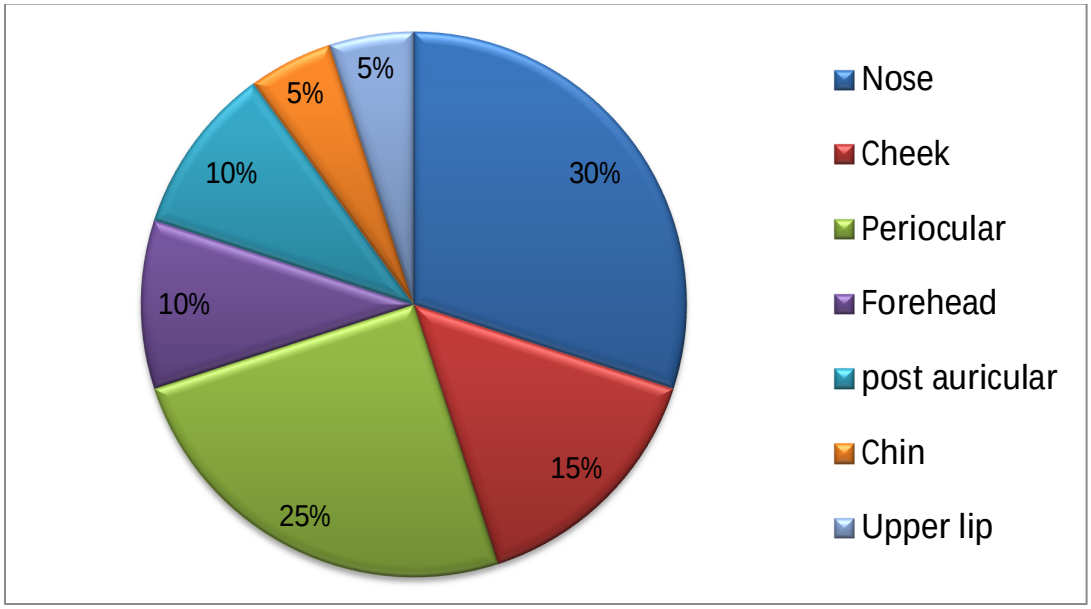
DISTRIBUTION OF BCC ACCORDING TO SITE

Distribution of lesions were confined to head and neck area. The most common site of involvement was nose (30%). It was followed by periocular area (25%), cheek (15%), forehead (10%), post auricular area (10%), upper lip (5%) and chin (5%).

Table 5: DISTRIBUTION OF BCC ACCORDING TO SITE

Site	No- 20
Nose	6
Periocular area	5
Cheek	3
Forehead	2
Post auricular area	2
Upper lip	1
Chin	1

Figure 5: DISTRIBUTION OF BCC ACCORDING TO SITE



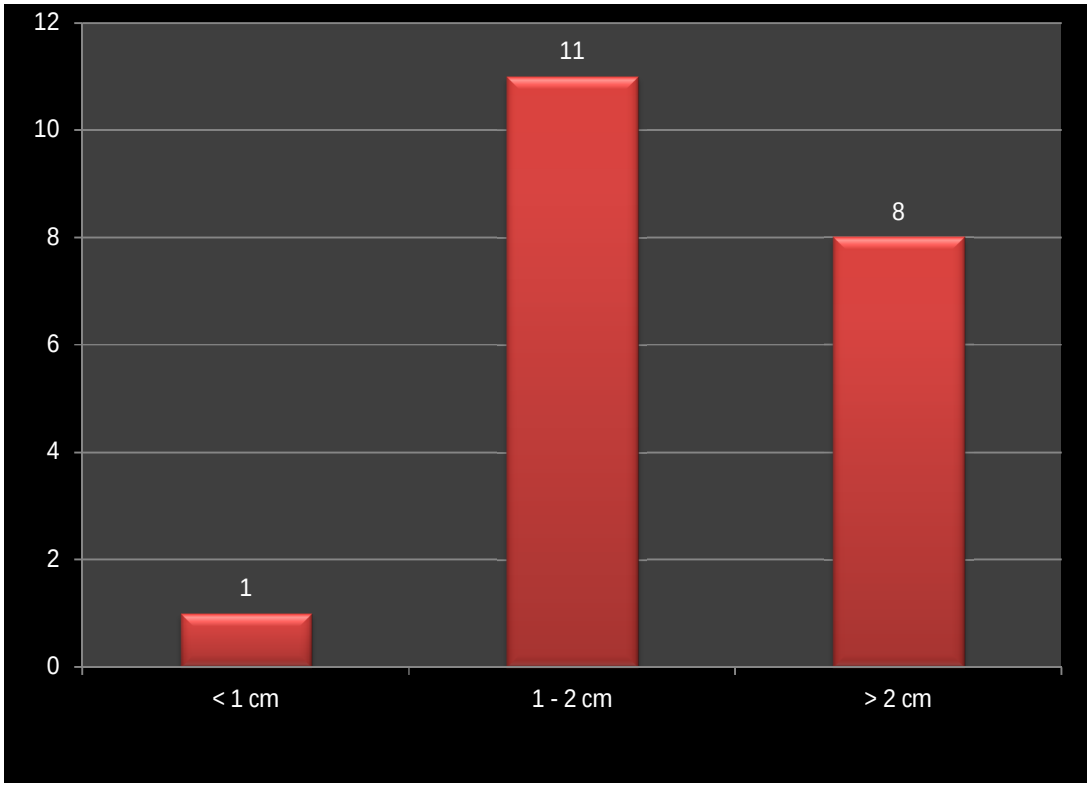
SIZE OF THE LESION

Most of the lesions lies between 1- 2 cm (55%) of size. It is followed by lesions with >2 cm size (40%) and <1cm in size (5%).

Table 6: SIZE OF THE LESION

Size of the lesion	No-20
Less than 1 cm	1
1 to 2 cm	11
More than 2 cm	8

Figure 6: SIZE OF THE LESION



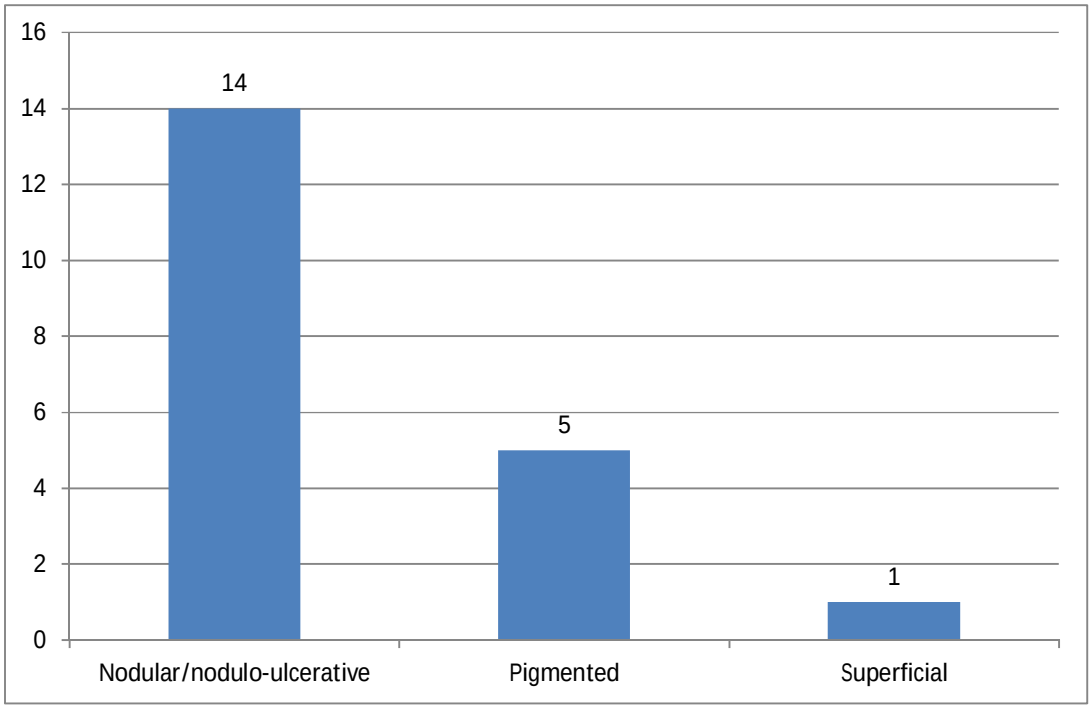
MORPHOLOGICAL TYPES OF BCC:

Most common morphological subtype of BCC was nodular / nodulo-ulcerative growth (70%). It was followed by pigmented varient (25%) and superficial BCC (5%).

Table 7: MORPHLOGICAL TYPES OF BCC

Morphology	No - 20	Percentage
Nodular / Nodulo-ulcerative	14	70%
Pigmented	5	25%
Superficial	1	5%

Figure 7: MORPHOLOGICAL TYPES OF BCC



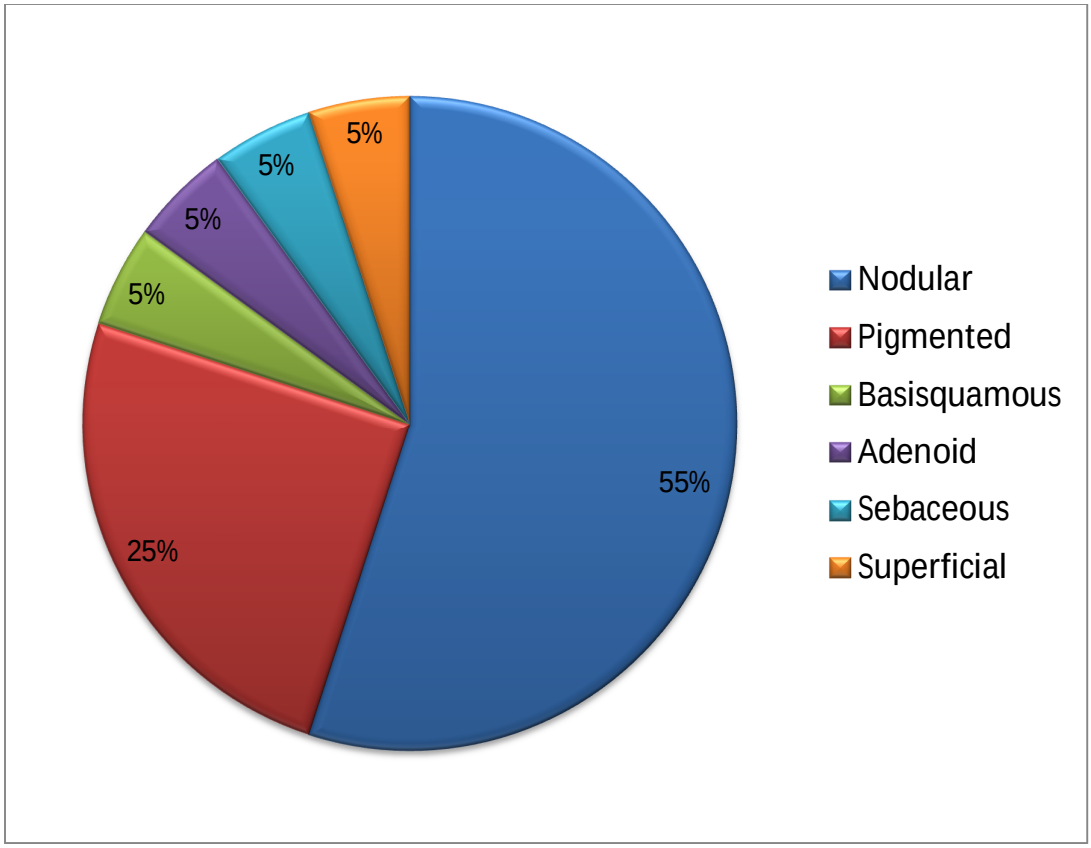
HISTOPATHOLOGICAL VARIANTS OF BCC:

The most common histopathological variant was Nodular subtype (55%) with significant proportion of tumors being pigmented (25%). Other subtypes included Basisquamous (5%), Adenoid variant (5%), BCC with sebaceous differentiation (5%) and Superficial BCC (5%).

Table 8: HISTOPATHOLOGICAL VARIANTS OF BCC

Histopathological variants	No – 20	Percentage
Nodular	11	55%
Pigmented	5	25%
Basisquamous	1	5%
Adenoid	1	5%
Sebaceous	1	5%
Superficial	1	5%

Figure 8: HISTOPATHOLOGICAL VARIANTS OF BCC



CLINICAL PICTURES

Figure (9) - Basisquamous carcinoma

A 65 year old female with nodulo-ulcerative growth on left cheek, histologically confirmed as Basisquamous carcinoma.

Figure (10)-Nodular BCC, pigmented variant

Figure (11) - Xeroderma pigmentosum

A 14 year old male patient with freckle like macules and atrophic depigmented macules on the sun exposed areas.

Figure (12)- Nodulo-ulcerative BCC

Same patient with nodulo – ulcerative plaque on right side of nose.

Figure (13) – Multiple BCC

A 57 year old male patient with multiple papules and plaques present on nose, cheek and periocular region. Some lesions shows surface ulceration.

Figure (14) - Superficial BCC

A 51 year old female patient, clinical picture shows annular plaque with beaded margin and surface ulceration.

HISTOPATHOLOGICAL PICTURES

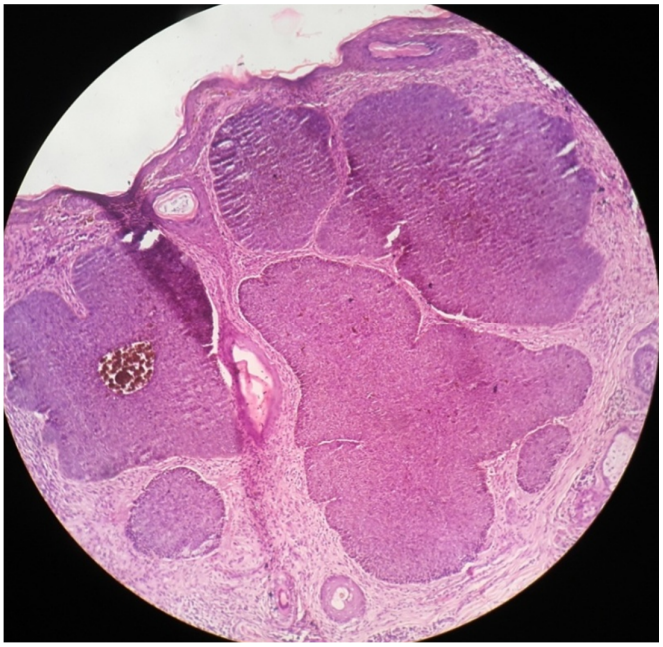


Figure (15)- Nodular basal cell carcinoma shows nodular tumor with peripheral palisading.

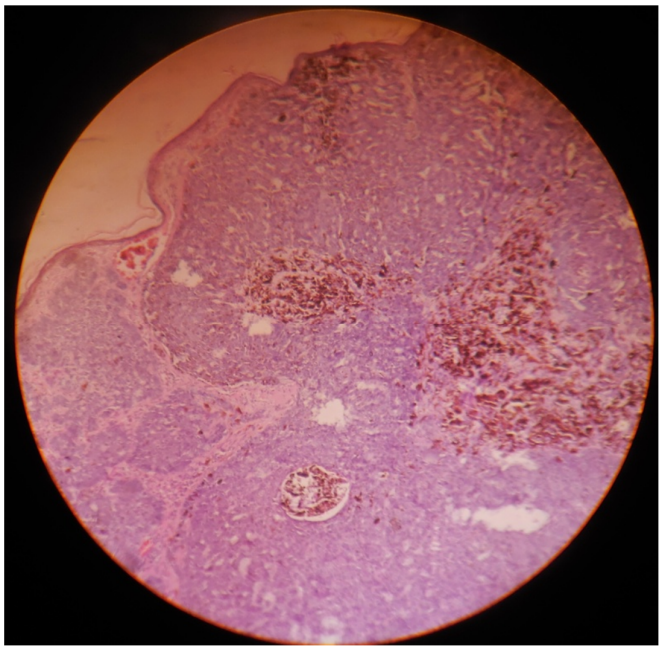


Figure (16) – Pigmented BCC

Melanin pigment is present within solid islands of basal cell carcinoma.

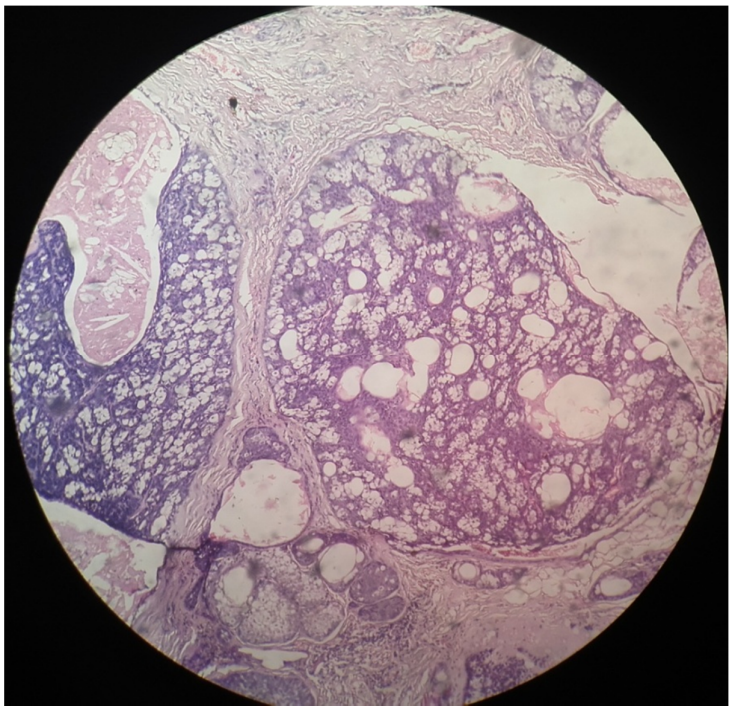


Figure (17) – Basal cell carcinoma with sebaceous differentiation.

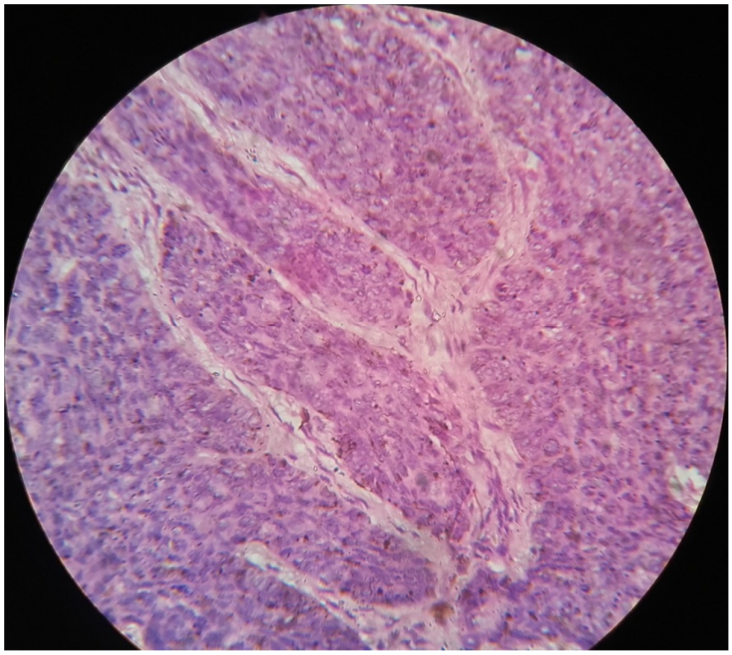


Figure (18) – Sebaceous BCC. High magnification.

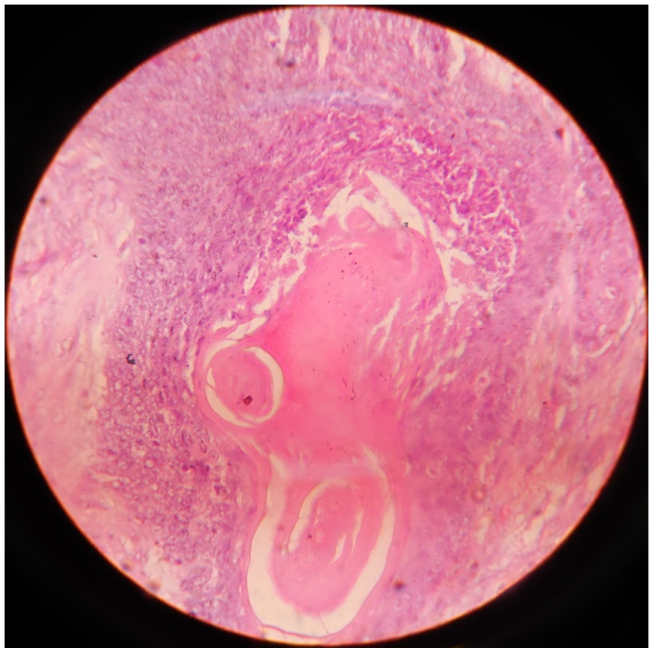


Figure (19) – Basisquamous carcinoma showing focal keratinization consisting of pearls with a colloidal center and an outer row of basaloid cells.

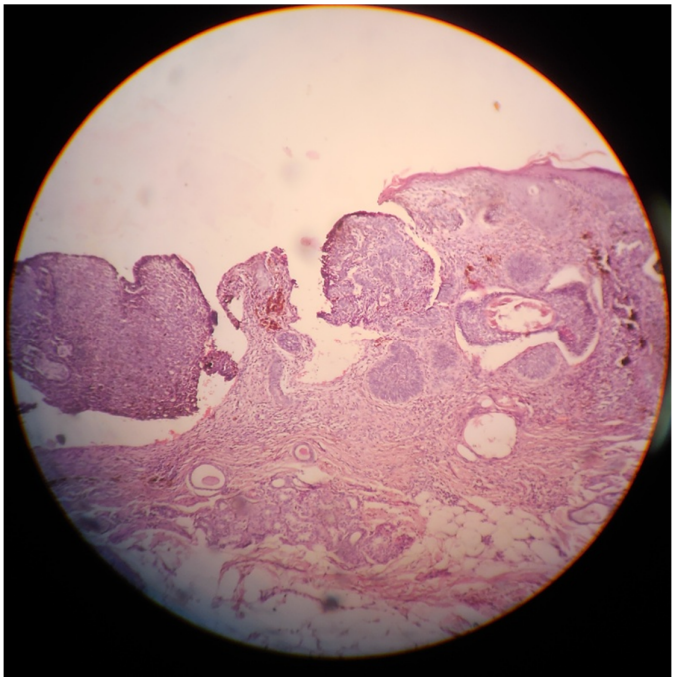


Figure (20) – Nodulo-ulcerative BCC shows epidermis with ulceration and neoplasm arising from basal layer arranged as clusters.

TREATMENT & FOLLOW-UP:

All the patients were treated by surgical exicision and cosmetic reconstruction was done by the plastic surgery department.

The patients were followed up every 6 months and further follow-up was also advised.

Discussion

DISCUSSION

In this study we included total of 20 patients with basal cell carcinoma. Among these 6 patients were males and 14 patients were females.

Sex distribution:

In our study, females were most commonly affected (70%) than males (30%) with a male to female ratio of 1: 2.33.

A study conducted by Laishram et al., 'pattern of skin malignancies in Manipur' which shows male to female ratio of 1: 2.[83] It is consistent with our study.

It is contrast to western studies, a study conducted by Sibel hakverdi, retrospective analysis of basal cell carcinoma showed male preponderance.[84]

BCCs are more common in males as reported in most studies worldwide, presumably due to greater occupational exposure to ultraviolet radiation (UVR). However, an unusual female preponderance was noticed in our study. Indian housewives especially rural women work in open kitchen during their household chores and work in the fields

during sowing and harvesting seasons exposing them to intermittent, high intensity UVR.

It might explain higher frequency of BCC in females in our study as intermittent rather than constant, cumulative UVR exposure is implicated in the pathogenesis of BCC. This female predilection may also be attributed to structurally thinner skin with lower collagen density in the dermis when compared to men.

Age distribution:

The most commonly affected age group in our study was 51 – 60 years (40%), followed by 61 – 70 years (30%) with a mean age of 56.7 years.

It is similar to a study conducted by Obaidullah and Aslam which showed a mean age of 56.3 years.[85]

Maximum age of the patient affected by BCC in our study was 72 years and the youngest age was 14 years.

Although basal cell carcinoma is rare in younger individuals, an increased incidence has also been noticed in children and young adults.[7]

Here we reported a 14 years old male patient with basal cell carcinoma and xeroderma pigmentosum.

Xeroderma pigmentosum is a rare autosomal recessive disease characterized by photosensitivity, pigmentary changes and early neoplasia resulting from abnormal DNA repair.

Our case presented with diffuse freckling on the face and nodular type of basal cell carcinoma on the right side of nose. (Figure -11)

This patient was treated by means of surgical exicision and reconstruction done at plastic surgery department. Also the patient was advised strict photo protective measures and regular follow up.

Higher rates of occurrence of BCC among elderly may be due to cumulative UVR induced DNA damage[86] as well as reduced efficiency of immune-surveillance and DNA repair mechanisms with aging.[87]

Duration of the disease:

Duration of the disease in our study ranging from 4 months to 5 years. Most of the cases (60%) in our study was reported with 6 months to 1 year duration.

The patients present at a later stage of the disease was attributable to lack of awareness about disease entity.

Long duration of the disease may lead to the following complications:

- Local invasion may leads to local tissue destruction and disfigurement
- Perineural invasion
- Metastasis

Distribution of BCC according to site:

The distribution of BCC in our study was confined head and neck area.

The most common site of involvement was nose (30%), followed by periocular area (25%) and cheek (15%).

It is similar to a study conducted by Malhotra et al., 'Basal cell carcinoma in the north Indian population' which showed head and neck being the commonest site (91.2%).[88]

Another study conducted by Asif et al., showed nose being the common site (28.9%) followed by eye (24.7%) and cheek (20.4%) which is closely resembles to our study.[89]

Size of the lesion:

Size of the lesions in our study ranged from as small as 0.5 cm to maximum of 6 cm.

Risk of metastases occur when tumor size is > 3 cm in diameter.

Risk of metastases related to tumor size:

3 cm – 1 – 2%

5 cm – 20 – 25%

>10 cm – 50%

It is also important to know the size of the tumor for TNM staging and therapeutic approach.

Morphological types of BCC:

The most common morphological sub type of BCC encountered in our study was nodular / nodulo-ulcerative type (70%), followed by pigmented BCC (25%) and superficial BCC (5%).

These findings are consistent with a study conducted by Sumirkumar et al., 'A study of basal cell carcinoma in south Asians' which showed common morphological subtype is being nodular / nodulo-ulcerative BCC (77.8%) and pigmented BCC (22.2%).[90]

Pain over the lesion was the chief complaint for eight patients and it was asymptomatic in twelve patients. Some patients had history of bleeding from minor trauma. None of them had any other systemic or cutaneous malignancies. There was no significant family history.

Nodular / nodulo-ulcerative BCC:

Patients with nodular type of BCC, having cutaneous features of skin coloured or hyperpigmented papules, nodules and plaques were present on head and neck area most commonly on nose, periocular and cheek. Some patients with nodulo-ulcerative lesions shows surface changes like ulceration and crusting.

Rare presentations:

- One 65 year old female patient was present with large nodulo-ulcerative growth (6×4 cm) on the left cheek of 2 years duration and later it was histopathologically diagnosed as basisquamous carcinoma. (Figure- 9)
- Another 57 year old male patient presented with multiple basal cell carcinomas as papules, nodules and plaques of varying sizes were present on the nose, cheek and preauricular region. (Figure-13).

Pigmented BCC:

Patients with pigmented BCC will be present as nodular lesions with grey-black pigmentation. In our study, 5 patients were appears clinically pigmented.

Superficial BCC:

Superficial BCC usually appear as erythematous, scaly patches that slowly increase in size by peripheral extension with fine thread like border.

The patches usually shows superficial ulceration, crusting and sometimes with central atrophic scarring.

Superficial BCC usually occurs on the trunk. But in our study 1 female patient was present with superficial BCC on forehead.(Figure 14)

Histopathological variants of BCC:

The most common histopathological variant in our study was nodular type (55%) with a significant proportion of tumors being pigmented (25%). Other subtypes included adenoid (5%), basisquamous (5%), superficial (5%) and BCC with sebaceous differentiation (5%).

These findings are closely resembles Malhotra et al., study which shows nodular type being the most common histologic variant (64.7%).[88]

Common histological features of basal cell carcinomas:

- Basaloid tumor cells
- Peripheral palisading of lesional cell nuclei
- Clefting artefact between the epithelium and stroma

Nodular BCC:

It was the most common histological subtype observed in our study. H &E stained smears showed nodules of basaloid cells with peripheral palisade arrangement and peritumoral lacunae were noted in all cases. Some cases shows cystic spaces within tumour masses.

Pigmented BCC:

It was the second most common histological subtype in our study. Histological features are resembles with nodular BCC, in addition there is presence of melanin within tumor cells and macrophages were noted in pigmented variant.

Superficial BCC:

One case presented with superficial BCC with typical features of buds and irregular proliferation of tumour tissue attached to the under surface of the epidermis.

Adenoid BCC:

This is the rare histopathological variant of BCC. Here we observed one case with Adenoid basal cell carcinoma. In this type tumor cells were arranged within clusters and focal lace like pattern of cells were made out.

BCC with sebaceous differentiation:

It is the another histological variant of BCC, which shows cystic spaces within the tumor lobules. Here one case presented clinically as nodular type of BCC and histology showed BCC with sebaceous differentiation.

Basisquamous carcinoma:

In our study we observed one rare case with histological findings suggestive of basisquamous carcinoma which was clinically appear as nodulo-ulcerative form of BCC.

Basisquamous carcinoma (BSC) is a rare epithelial neoplasm with histological features of both basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) and it is linked by a transition zone. It is also known as metatypical epitheliomas.

Most common location of BSC is on the head and neck and mainly involving the central face and has a significant male predominance.

In contrast to pure BCC, basaloid cells in basisquamous carcinoma have eosinophilic cytoplasm, often with lack of peripheral palisading and retraction artifact and may exhibit cytoplasmic keratinization.

SCC areas are characterized by large polygonal squamoid cells with eosinophilic cytoplasm and may reflect cytoplasmic keratinization.

Like squamous cell carcinoma, basisquamous carcinoma also more aggressive and locally invasive . Risk of metastasis is more in BSC than forms of BCC.

Metastatic BSC is difficult to treat and its prognosis is poor.

Summary

SUMMARY

- In our study out of 20 patients of basal cell carcinoma 6 were males and 14 were females.
- Females were most commonly affected than males.
- Male to female ratio – 1: 2.33.
- Most commonly affected age group was 50 – 70 years.
- Distribution of basal cell carcinoma in our study was confined to head and neck area. Most common site of involvement was nose, followed by periocular region and cheek.
- Most common morphological subtype encountered in our study was Nodular / nodulo-ulcerative BCC, followed by pigmented variant.
- Most common histological variant observed in our study was nodular type, followed by pigmented variant.

Rare presentations observed in our study:

- Xeroderma pigmentosum with basal cell carcinoma.
- Multiple basal cell carcinoma
- Basisquamous carcinoma
- Histological variants of BCC includes adenoid and sebaceous differentiation.

Conclusion

CONCLUSION

- This study highlights a paradoxically increasing trend of BCC with female predilection.

- Since early age of onset of basal cell carcinoma being reported in persons with genetic defect, these patients should be advised for periodic follow up and strict photo protective measures.

- Early detection and treatment of lesions are crucial to decrease functional and cosmetic morbidity and costs, this study highlights the importance of improving awareness among general practitioners, public health workers and general population.

- The clinical and epidemiological data collected in this study would serve as a reference for future research and may be helpful in the development of preventive and educational strategies.

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Annexures

ABBREVIATIONS

1.	BCC	–	Basal cell carcinoma
2.	SCC	–	Squamous cell carcinoma
3.	BSC	–	Basisquamous carcinoma
4.	UVR	–	Ultraviolet rays
5.	PTCH1 gene	–	Protein patched homolog 1 gene
6.	TNF-α	–	Tumour necrosis factor – α
7.	IL-10	–	Interleukin-10
8.	XP	–	Xeroderma pigmentosum
9.	NER	–	Nucleotide excision repair
10.	PNI	–	Perineural invasion
11.	MMS	–	Mohs' micrographic surgery
12.	C & D	–	Curettage & Desiccation
13.	5-FU	–	5-Fluorouracil
14.	PDT	–	Photodynamic therapy
15.	H & E	–	Haematoxylin and Eosin

MASTER CHART

S. No	Name	Age	Sex	Site	Clinical Type	Histological Type
1.	Suseela	72	F	Chin	Nodulo-ulcerative	Nodular
2.	Punithavathy	61	F	Nose	Nodular	Adenoid
3.	Saroja	65	F	Cheek	Nodulo-ulcerative	Basisquamous
4.	Pappammal	60	F	Upper lip	Nodulo-ulcerative	Nodular
5.	Kamaladevi	65	F	Post auricular region	Pigmented	Pigmented
6.	Nirmalkumar	14	M	Nose	Nodular	Nodular
7.	Mylammal	60	F	Cheek	Nodular, pigmented	Pigmented
8.	Valli	55	F	Forehead	Nodular	Sebaceous
9.	Purusothaman	35	M	Post auricular region	Pigmented	Pigmented
10.	Sekar	57	M	Nose,cheek	Nodular	Nodular
11.	Ayesa bee	66	F	Periocular	Nodulo-ulcerative	Nodular
12.	Kizhiyappan	45	M	Nose	Pigmented	Pigmented
13.	Krishna	72	F	Cheek	Nodular	Nodular
14.	Abdulkathar	60	M	Periocular	Nodulo-ulcerative	Nodular
15.	Rajalakshmi	65	F	Nose	Nodulo-ulcerative	Nodular
16.	Kothandapani	40	M	Periocular	Nodulo-ulcerative	Nodular
17.	Vendavirudham	65	F	Periocular	Nodulo-ulcerative	Pigmented
18.	Indrani	60	F	Nose	Nodulo-ulcerative	Nodular
19.	Prema	51	F	Periocular	Nodular	Nodular
20.	Glory jemima	51	F	Forehead	Superficial	Superficial

S.No – Serial number, M – Male, F – Female

PROFORMA

Name: Age: Sex: M / F

Hospital No.: Occupation:

Address:

COMPLAINTS

Skin lesion

Site

Duration

Associated symptoms: Pain / Itching / Altered sensation / Discharge / Colour change / Crusting / Bleeding

Systemic symptoms:

Past / treatment history:

Personal / Family history:

Exposure: Sun / Chemicals / Radiation

GENERAL EXAMINATION

Built:

Pallor: Icterus:Fever:

Other findings:

PR: BP: _____ mmHg Temp:1

SYSTEMIC EXAMINATION

CVS:

RS:

Abdomen:

CNS:

D/E: Primary lesion

Macule / Papule / Patch / Nodule / Ulcer / Others

Site	:	Size	:
Number	:	Shape	:
Pigmentation	:	Colour	:
Erythema	:	Linearity	:

Surface	:	Flat topped	Elevated	Raised
		Papillomatous	Smooth	Shiny
		Verrucous	Fungoid	Indurated
		Scaling	Crusting	Ulceration
		Nodular	Telangiectasia	

Sessile : Pedunculated :

Dome-shaped : Umbilication :

Borders/margins : Base :

Warmth : Tenderness :

Bleeds on touch :

Consistency : Soft / Cystic / Firm / Hard

Attachment to underlying structures :

Regional lymph node enlargement :

Any other site with similar lesion :

Other associated findings :

Scalp :

Hair :

Oral mucosa :

INVESTIGATIONS

Blood CBC	BT	CT	RBS
	HIV 1&2 antibodies		VDRL

X-ray chest

SKIN BIOPSY Biopsy No. : Date:

Site :

Report :

Therapy :

Follow Up :

INFORMATION TO PARTICIPANTS

Title : **BASAL CELL CARCINOMA – A PROSPECTIVE CLINICO EPIDEMIOLOGICAL & PATHOLOGICAL STUDY**

Principal Investigator : Dr. AMMASAIGOUNDAN.V
Co-Investigator(if any) :
Name of Participant :

Site :

You are invited to take part in this study. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns.

What is the purpose of research?

Basal cell carcinoma is a slow growing malignant tumour of skin. We are doing a study to identify the various morphological and histopathological features of basal cell carcinoma. This would help us diagnose and treat these tumours effectively.

We have obtained permission from the Institutional Ethics Committee.

The study design

All the patients presenting to the dermatology OPD of RGGGH, with Basal cell carcinoma are included in this study.

Study Procedures

The study involves a thorough history and clinical examination. A detailed dermatological examination pertaining to the tumour is done. Routine blood investigations like Complete haemogram, Random blood sugar are done.

After the evaluation, the tumours are subjected to incision / excision biopsy under local anaesthesia after giving Inj. Xylocaine 2% (local anaesthetic agent) test dose and Inj.Tetanus toxoid. The excised specimen is sent for routine histopathological examination. This biopsy is a part of the treatment for these skin tumours and also provides more information on the type of tumour and aid in further management. You have to review after 1 week for examination of the biopsy site, suture removal and collection of the histopatholgy reports.

Possible risks to you – Biopsy done in the study is a part of the treatment. Some may develop allergy to the local anaesthetic agent used for local anaesthesia. It is used only after giving test dose. The procedure is done under strict aseptic precautions and there is very minimal negligible chances for wound infection.

Possible benefits to you – Excision biopsy done is curative for most of the tumours.

Possible benefits to other people

The results of the study may provide benefits to the society in terms of advancement of medical knowledge and/or therapeutic benefit to future patients.

Confidentiality of the information obtained from you

You have the right to confidentiality regarding the privacy of your medical information (personal details, results of physical examinations, investigations, and your medical history). By signing this document, you will be allowing the research team investigators, other study personnel, sponsors, Institutional Ethics Committee and any person or agency required by law like the Drug Controller General of India to view your data, if required.

The information from this study, if published in scientific journals or presented at scientific meetings, will not reveal your identity.

How will your decision to not participate in the study affect you?

Your decision not to participate in this research study will not affect your medical care or your relationship with the investigator or the institution. You will be taken care of and you will not loose any benefits to which you are entitled.

Can you decide to stop participating in the study once you start?

The participation in this research is purely voluntary and you have the right to withdraw from this study at any time during the course of the study without giving any reasons. However, it is advisable that you talk to the research team prior to stopping the treatment/discontinuing of procedures etc.

Signature of Investigator	Signature of Participant
Date	Date

PATIENT CONSENT FORM

Title of the study :BASAL CELL CARCINOMA – A PROSPECTIVE CLINICO EPIDEMIOLOGICAL & PATHOLOGICAL STUDY

Name of the Participant:

Name of the Principal(co-investigator): Dr.Ammasaigoundan.V

Name of the Institution: Department of Dermatology, Rajiv Gandhi Government General Hospital, Chennai.

Documentation of the informed consent

I _____ have read the information in this form (or it has been read for me). I was free to ask any questions and they have been answered. I am over 18 years of age and exercising my free power of choice, hereby give my consent to be included as a participant in the study (or) I hereby give my consent to include my Son / daughter as a participant in this study.

1. I have read and understood this consent form and the information provided to me.
2. I have had the consent document explained to me.
3. I have been explained about the nature of the study.
4. My rights and responsibilities have been explained to me by the investigator.
5. I agree to cooperate with the investigator and I will inform him/her immediately if I suffer unusual symptoms.
6. I have not participated in any research study at any time .
7. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.
8. I hereby give permission to the investigators to release the information obtained from me as a result of participation in this study to the sponsors, regulatory authorities, Govt. agencies and IEC. I understand that they are publicly presented.
9. My identity will be kept confidential if my data are publicly presented.
10. I am aware that if I have any question during this study, I should contact at one of the addresses listed above. By signing this consent form I attest that the information given in this document has been clearly explained to me and apparently understood by me. I will be given a copy of this consent document.

Participant's initials:_____

For adult participants:

Name and signature/thumb impression of the participant (or legal representative if participant incompetent)

_____	_____	_____
Name	Signature	Date

Name and signature of impartial witness (required for illiterate patients):

_____	_____	_____
Name	Signature	Date

Address and contact number of the impartial witness:
Name and Signature of the investigator or his representative obtaining consent:

_____	_____	_____
Name	Signature	Date

ஆராய்ச்சி தகவல் தாள்

பங்கேற்பாளர்கள் தகவல்
தலைப்பு
முக்கிய ஆராய்ச்சியாளர்
துணை ஆராய்ச்சியாளர்
பங்கேற்பாளர் பெயர்

இந்த ஆய்வில் பங்கேற்க தங்களை அழைக்கிறோம். இந்த ஆவணத்தில் உள்ள தகவல் நீங்கள் பங்கேற்க வேண்டுமா அல்லது வேண்டாமா என முடிவு எடுக்க உதவுவதாக அமையும். நீங்கள் எந்த கேள்விகள் அல்லது கருத்துகள் இருந்தால் கேட்க தயங்க வேண்டாம்.

இந்த ஆய்வின் நோக்கம் என்ன?
தோல் புற்று நோய் ஒரு பொதுவான சரும நோய். இந்த நோயின் பல்வேறு விதங்கள், உருவ மாற்றங்கள் மற்றும் திசு நுண்ணியல் வேறுபாடுகள் கண்டறிவதே இந்த ஆராய்ச்சியின் நோக்கமாகும். இது எங்களுக்கு இந்த கட்டிகளை திறம்பட கண்டறிய மற்றும் புற்று நோய் சிகிச்சை தர உதவும். நாங்கள் இதற்கு நிறுவன நெறிமுறைகள் குழு அனுமதி பெற்றுள்ளோம்.

ஆய்வு வடிவமைப்பு:
சென்னை ராஜிவ் காந்தி அரசு பொது மருத்துவமனை தோல் நோய் புற நோயளிகள் பிரிவுக்கு வரும் தோல் புற்றுநோய் உள்ள நோயாளிகள் இந்த ஆராய்ச்சியில் சேர்த்துக்கொள்ளப்படுவார்கள்.

ஆய்வு நடைமுறைகள்:
ஆய்வுக்கு முதலில் ஒரு முழுமையான நோய் வரலாறு மற்றும் உடல் பரிசோதனை செய்யப்படும். பிறகு முழுமையான தோல் மற்றும் கட்டி பரிசோதனை செய்யப்படும். பின் வழக்கமான இரத்த பரிசோதனை செய்யப்படும்.
மதிப்பீட்டிற்கு பின் டெட்டானஸ் மற்றும் மருப்பு ஊசி கொடுத்து கட்டிகள் கீறல் / வெட்டி எடுக்கும் திசு ஆய்வுக்கு உட்படுத்தப்படும். அகற்றப்பட்ட கட்டிகள் வழக்கமான திசு பரிசோதனைக்கு அனுப்பப்படும். இந்த திசு பரிசோதனை இந்த தோல் கட்டிகளுக்கு ஒரு சிகிச்சை நடைமுறையாகவும், மற்றும் கட்டியின் வகையை கண்டறிய ஏதுவாகவும் உள்ளது. ஒரு வாரம் கழித்து மறு பரிசீலனைக்கு மற்றும் தையல் அகற்ற வரவேண்டும். அதன் பிறகு திசு பரிசோதனை முடிவுகளையும் பெற்றுக்கொள்ளலாம்.

உங்களுக்கு சாத்தியமுள்ள இடர்பாடுகள்: கட்டி அகற்றும் சிகிச்சை மற்றும் திசு பரிசோதனை இந்த சிகிச்சையின் பகுதிகளாகும். இதில் தாங்களுக்கு மருப்பு மருந்திற்கு ஒவ்வாமை மற்றும் காயத்தில் தொற்று ஏற்பட வாய்ப்புள்ளது. இவை ஏற்படாமல் இருக்க முன்னெச்சரிக்கை எடுத்துக்கொள்ளப்படுகிறது.

உங்களுக்கு சாத்தியமுள்ள நன்மைகள்: கட்டி திசு பரிசோதனைக்கு அகற்றப்படுவது பிணி நீக்கும் பாங்குடையது.

மற்ற மக்களுக்கு சாத்தியமுள்ள நன்மைகள்: ஆய்வு முடிவுகள் எதிர்கால நோயாளிகளுக்கு தோல் புற்றுநோய் மற்றும் சிகிச்சை குறித்த விழிப்புணர்வை மக்களுக்கு ஏற்படுத்த உதவும்.

உங்களிடம் இருந்து பெறப்பட்ட தகவல் இரகசியத்தன்மை: உங்கள் மருத்துவ தகவல்கள் தனியுரிமை தொடர்பான இரகசியத்தன்மை உரிமை உங்களுக்கு உண்டு. இந்த ஆவணத்தில் கையெழுத்திட்டு, நீங்கள் தேவையான ஆராய்ச்சி குழு விசாரணை, மற்ற ஆய்வு பணியாளர்கள், விளம்பரதாரர்கள், நிறுவன நெறிமுறைகள் குழு மற்றும் உங்கள் தரவு பார்வையிட இந்திய மருந்து கட்டுப்பாட்டு ஜெனரல் போன்ற சட்டம் தேவை என்று கூறும் ஆட்கள் உங்களின் விவரங்களை ஆராய அனுமதி அளிக்கிறீர்கள். இந்த ஆய்வு தகவல், அறிவியல் பத்திரிகைகளில் வெளியிடப்பட்ட அல்லது அறிவியல் கூட்டங்களில் வழங்கினார் என்றால், உங்கள் அடையாளத்தை வெளிப்படுத்த மாட்டேன்.

எப்படி ஆய்வில் பங்கேற்க முடியாது என்ற உங்கள் முடிவை அது பாதிக்கும்? இந்த ஆராய்ச்சியில் பங்கு கொள்ள விருப்பம் இல்லையெனினும் அது உங்களது மருத்துவ பரிசீலனை மற்றும் சிகிச்சைக்கு எந்த ஒரு பாதிப்பும் உண்டாக்காது.

இந்த ஆய்விலிருந்து நடுவில் விலகிக்கொள்ள முடியுமா? இதில் பங்கு கொள்வது முற்றிலும் உங்கள் விருப்பம். நடுவில் விலக விரும்பினால் தாராளமாக விலகிக்கொள்ளலாம். எனினும், அதை நீங்கள் சிகிச்சையை நிறுத்தாமல் /இடையில் நிறுத்தும் முன்னர் ஆராய்ச்சி குழுவிடம் பேசி முடிவெடுக்கவும் என்று அறிவுறுத்தப்படுகிறது.

ஆராய்ச்சியாளர் கையொப்பம் **பங்கேற்பாளர் கையொப்பம்**

தேதி **தேதி**

ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சி தலைப்பு: தோல் புற்றுநோய் பற்றிய ஆராய்ச்சி

பெயர்: **தேதி:**
வயது: **உள்நோயாளி எண்:**
பால்: **ஆராய்ச்சி சேர்க்கை எண்:**

இடம்: தோல் நோய் பிரிவு, ராஜீவ் காந்தி அரசு பொது மருத்துவமனை.

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது.

எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்து கொண்டு நான் எனது சம்மதத்தை தெரிவிக்கிறேன்.

எனக்கு வயது 18க்கு மேல் ஆகிறது / 18 வயதுக்கு உட்பட்ட எனது மகன்/மகள் இந்த ஆராய்ச்சியில் பங்கு கொள்ள எனக்கு சம்மதம்.

எனக்கு தோலில் தசை / திசு பரிசோதனை செய்து கொள்ள சம்மதம்.

இந்த ஆரய்ச்சியில் பிறரின் நிர்ப்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில் தான் பங்கு பெறுகிறேன் மற்றும் நான் இந்த ஆராய்ச்சியிலிருந்து எந்நேரமும் பின்வாங்கலாம் என்பதையும் அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் நான் புரிந்துகொண்டேன்.

நான் இந்த ஆராய்ச்சியின் விவரங்களை கொண்ட தகவல் தாளைப் பெற்றுக்கொண்டேன்.

நான் என்னுடைய சுயநினைவுடன் மற்றும் முழுசுதந்திரத்துடன் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக்கொள்ள சம்மதிக்கிறேன்.

எனக்கு நோய்க்குறியியல் துறையில் தோல், தசை மற்றும் திசு பரிசோதனைக்கு பயன்பட்ட மெழுகுக்கட்டிகளை வைத்து ஆராய்ச்சி மற்றும் சிறப்பு பரிசோதனை செய்து கொள்ள சம்மதம் தெரிவிக்கிறேன்.

இந்த ஆராய்ச்சியின் முடிவுகளை வெளியிடலாம். அப்படி வெளியிட்டால், எனது அடையாளம் ரகசியமாக வைக்கப்படும் எனபதன் பேரில் அதற்கு சம்மதம் தெறிவிக்கிறேன்.

ஆராய்ச்சியாளர் கையொப்பம் **பங்கேற்பாளர் கையொப்பம்**

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No. 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. Ammasaigoundan.V
Postgraduate M.D.(DVL),
Madras Medical College,
Chennai – 600 003.

Dear Dr. Ammasaigoundan.V,

The Institutional Ethics Committee has considered your request and approved your study titled **"BASAL CELL CARCINOMA – A PROSPECTIVE CLINICO EPIDEMIOLOGICAL & PATHOLOGICAL STUDY". No.26112014.**

The following members of Ethics Committee were present in the meeting held on 11.11.2014 conducted at Madras Medical College, Chennai-3.

1. Dr.C.Rajendran, M.D.,	: Chairperson
2. Dr.R.Vimala, M.D., Dean, MMC, Ch-3	: Deputy Chairperson
3. Prof.B.Kalaiselvi, M.D., Vice-Principal, MMC, Ch-3	: Member Secretary
4. Prof.R.Nandini, M.D., Inst.of Pharmacology, MMC	: Member
5. Prof.P.Ragumani, M.S., Professor, Inst.of Surgery, MMC	: Member
6. Prof.Md.Ali, M.D., D.M., Prof. & HOD of Medl.G.E., MMC	: Member
7. Prof.K.Ramadevi, Director i/c, Inst.of Biochemistry, MMC	: Member
8. Prof.Saraswathy, M.D., Director, Pathology, MMC, Ch-3	: Member
9. Prof.S.G.Sivachidambaram, M.D., Director i/c, Inst.of Internal Medicine, MMC	: Member
10. Thiru S.Rameshkumar, Administrative Officer	: Lay Person
11. Thiru S.Govindasamy, B.A., B.L.,	: Lawyer
12. Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

24/11/14

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003